



Title	NOVEL HUMAN VIRUS CAUSING RESPIRATORY TRACT INFECTION AND USES THEREOF
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(19) **United States**(12) **Patent Application Publication****YUEN et al.**(10) **Pub. No.: US 2009/0305282 A1**(43) **Pub. Date: Dec. 10, 2009**(54) **NOVEL HUMAN VIRUS CAUSING
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Jul. 21, 2004, now Pat. No. 7,553,944.**Publication Classification**(51) **Int. Cl.**
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(52) **U.S. Cl.** **435/6**
(57) **ABSTRACT**

The present invention provides the complete genomic sequence of a novel human coronavirus, coined as coronavirus-HKU1 ("CoV-HKU1"), isolated in Hong Kong from a patient who had a recent history of visit to Schenzhen. China. The virus belongs to the order Nidovirales of the family Coronaviridae, being a single-stranded RNA virus of positive polarity. The invention also provides the deduced amino acid sequences of the complete genome of the CoV-HKU1. The nucleotide sequences and deduced amino acid sequences of the CoV-HKU1 are useful in preventing, diagnosing and/or treating the infection by CoV-HKU1. Furthermore, the invention provides immunogenic and vaccine preparations using recombinant and chimeric forms as well as subunits of the CoV-HKU1 based on the nucleotide sequences and deduced amino acid sequences of the CoV-HKU1.

SEQ:1	1	TCGTGCTATGCCAAATATTTTGCCTATTGTTAGTAGTTTAGTTTGGCCCGCAAACAT	58
SEQ:2	1	R A M P N I L R I V S S L V L A R K H	19
	59	GAATTTTGTGTTTACATGGTGATAGATTTTATCGCCTTGCGAATGAATGTGCTCAAGTT	118
	20	E F C C S H G D R F Y R L A N E C A Q V	39
	119	TTGAGTGAAATAGTTATGTGTGCGGTTGCTATTATGTTAAGCCTGGTGGTACTAGCAGT	178
	40	L S E I V M C G G C Y Y V K P G G T S S	59
	179	GGTGATGCAACTACTGCTTTTGCTAATTCTGTTTTTAATATATGTCAGGCTGTTACTGCT	238
	60	G D A T T A F A N S V F N I C Q A V T A	79
	239	AATGTTTGTTCCTTATGGCCTGTAATGGCCATAAGATTGAAGATTTAAGTATACGCAAT	298
	80	N V C S L M A C N G H K I E D L S I R N	99
	299	TTACAAAACGCTTATACTCTAATGTTTATCGTACAGATTATGTTGATTATACATTTGTT	358
	100	L Q K R L Y S N V Y R T D Y V D Y T F V	119
	359	AATGAGTATTATGAATTTTATGTAAGCATTTTAG	393
	120	N E Y Y E F L C K H F	130

FIG. 1

SEQ:3 1 GAATAAGAGCGAATTGCGTCCGTACCGTCTATCAGCTTACGATCTCTTGTGAGATCTCAT 60
E * E R I A S V P S I S L R S L V R S H
N K S E L R P Y R L S A Y D L L S D L I
I R A N C V R T V Y Q L T I S C Q I S

61 TAAATCTAAACTTTTAAACAAGATTCCCTGTTATCCATGCTTGTGAGTGTGGTTAATC 120
* I * T F * T R F P V I H A C E C G L I
K S K L F K Q D S L L S M L V S V V * S
L N L N F L N K I P C Y P C L * V W F N

121 ATAATCTTGTATTTTACTTTCCACACTTTTCATCTCTCTGCCAGTGACGTGTTGTTGTC 180
I I L Y F T F H T F H L S A S D V L V V
* S C I L L S T L F I S L P V T C W L S
H N L V F Y F P H F S S L C Q * R V G C

181 CTCAGCGTCCCTCCCATAGGTCGCAATGATTAACCAGCAAATACGGTCTCGGCTTCAA 240
L S V P P I G R N D * N Q Q I R S R L Q
S A S L P * V A M I K T S K Y G L G F K
P Q R P S H R S Q * L K P A N T V S A S

241 GTGGGCGCCAGAATTTGCTGGCTGCTCCGGATGCAGCGGAGGAGTTGGCTAGTCTCTAT 300
V G A R I S L A A S G C S G G V G * S Y
W A P E F R W L L P D A A E E L A S P M
S G R Q N F V G C F R M Q R R S W L V L

301 GAAGTCAGATGAGGGTGGGTTATGCCCTCTACTGGTCAAGCGATGAAAGTGTGGATT 360
E V R , * G W V M P L Y W S S D G K C W I
K S D E G G L C P S T G Q A M E S V G F
* S Q M R V G Y A P L L V K R W K V L D

361 CGTTTATGATAATCATGTGAAGATAGATTGTCGCTGCATTCTTGGACAAGAATGGCATGT 420
R L * * S C E D R L S L H S W T R M A C
V Y D N H V K I D C R C I L G Q E W H V
S F M I I M * R * I V A A F L D K N G M

421 GCAGTCAAATCTTATCCGTGATATTTTGTTCATGAAGATCTACATGTTGTAGAAGTTCT 480
A V K S Y P * Y F C S * R S T C C R S S
Q S N L I R D I F V H E D L H V V E V L
C S Q I L S V I F L F M K I Y M L * K F

481 AACTAAACAGCCGTAAAGTCCGGTACGGCAATTTTAATTAAATCACCTTTGCATAGCTT 540
N * N S R K V R Y G N F N * I T F A * L
T K T A V K S G T A I L I K S P L H S L
* L K Q P * S P V R Q F * L N H L C I A

FIG. 2

541 GGGTGGTTTTCTAAAGGGTATGTTATGGGCTTGTTCGGTTCATACAAGACTAAACGTTA 600
 G W F S * R V C Y G L V P F I Q D * T L
 G G F P K G Y V M G L F R S Y K T K R Y
 W V V F L K G M L W A C S V H T R L N V

601 TGGTGTACATCATCTTTCTATGACTACATCTACTACTAATTTGGTGAAGATTTTTTGGG 660
 C C T S S F Y D Y I Y Y * F W * R F F G
 V V H H L S M T T S T T N F G E D F L G
 M L Y I I F L * L H L L L I L V K I F W

661 TTGGATTGTACCTTTTGGTTTTATGCCATCTTATGTTCCAAATGGTTTCAATTCTGTAG 720
 L D C T F W F Y A I L C S Q M V S I L *
 W I V P F G F M P S Y V H K W F Q F C R
 V G L Y L L V L C H L M F T N G F N S V

721 GTTGTATATTGAAGAGAGTGATTAAATAATTTCAAATTTTAAATTTGATGATTATGATTT 780
 V V Y * R E * F N N F K F * I * * L * F
 L Y I E E S D L I I S N F K F D D Y D F
 G C I L K R V I * * F Q I L N L M I M I

781 TAGTGTAGAAGATGCTTATGCTGAGGTTTCATGCTGAGCCTAAAGGTAAATATTCACAAAA 840
 * C R R C L C * G S C * A * R * I F T K
 S V E D A Y A E V H A E P K G K Y S Q K
 L V * K M L M L R F M L S L K V N I H K

841 AGCTTATGCTTTACTTAGACAATATCGTGGTATTAAACCCGTACTTTTTGTAGACCAGTA 900
 S L C F T * T I S W Y * T R T F C R P V
 A Y A L L R Q Y R G I K P V L F V D Q Y
 K L M L Y L D N I V V L N P Y F L * T S

901 TGGTGTGACTATTCTGGTAAATTAGCAGATTGTCTTCAAGCTTATGGTCATTATTCTTT 960
 W L * L F W * I S R L S S S L W S L F F
 G C D Y S G K L A D C L Q A Y G H Y S L
 M V V T I L V N * Q I V F K L M V I I L

961 GCAAGATATGAGACAAAAGCAGTCTGTATGGCTTGCCAATTGTGACTTTGATATTGTAGT 1020
 A R Y E T K A V C M A C Q L * L * Y C S
 Q D M R Q K Q S V W L A N C D F D I V V
 C K I * D K S S L Y G L P I V T L I L *

1021 GGCTTGGCATGTAGTTCGTGATTACGATTTGTTATGCGCCTGCAGACTATAGCTACTAT 1080
 G L A C S S * F T I C Y A P A D Y S Y Y
 A W H V V R D S R F V M R L Q T I A T I
 W L G M * F V I H D L L C A C R L * L L

FIG. 2 CONT.

1081 TTGTGGTATTAAATATGTTGCACAACCTACAGAAGATGTAGTAGATGGAGATGTAGTTAT 1140
 L W Y * I C C T T Y R R C S R W R C S Y
 C G I K Y V A Q P T E D V V D G D V V I
 F V V L N M L H N L Q K M * * M E M * L

1141 ACGTGAACCTGTACATTTATTATCTGCTGATGCAATAGTTTAAAGCTTCCTAGTTTGAT 1200
 T * T C T F I I C * C N S F K A S * F D
 R E P V H L L S A D A I V L K L P S L M
 Y V N L Y I Y Y L L M Q * F * S F L V *

1201 GAAAGTTATGACTCATATGGATGATTTTTCTATTAAATCTATATATAATGTTGATTGTG 1260
 E S Y D S Y G * F F Y * I Y I * C * F V
 K V M T H M D D F S I K S I Y N V D L C
 * K L * L I W M I F L L N L Y I M L I C

1261 TGATTGTGGTTTTGTTATGCAGTATGGTTATGTAGATTGTTTAAATGATAATTGTGATTT 1320
 * L W F C Y A V W L C R L F * * * L * F
 D C G F V M Q Y G Y V D C F N D N C D F
 V I V V L L C S M V M * I V L M I I V I

1321 TTATGGTTGGGTTTCAGGTAATATGATGGATGGTTTTCTTGTCCATTGTGTTGTACAGT 1380
 L W L G F R * Y D G W F F L S I V L Y S
 Y G W V S G N M M D G F S C P L C C T V
 F M V G F Q V I * W M V F L V H C V V Q

1381 TTATGACTCTAGCGAAGTTAAAGCCCAATCATCTGGTGTATTCCCTGAAAATCCTGTGTT 1440
 L * L * R S * S P I I W C Y S * K S C V
 Y D S S E V K A Q S S G V I P E N P V L
 F M T L A K L K P N H L V L F L K I L C

1441 ATTTACTAATAGTACTGATACTGTTAACCATGATTCTTTTAATTGTATGGTTATTCTGT 1500
 I Y * * Y * Y C * P * F F * F V W L F C
 F T N S T D T V N H D S F N L Y G Y S V
 Y L L I V L I L L T M I L L I C M V I L

1501 CACACCATTTGGTTCTTGTATATATTGGTCGCCGCTCCTGGATTGTGGATTCCTATAAT 1560
 H T I W F L Y I L V A A S W I V D S Y N
 T P F G S C I Y W S P R P G L W I P I I
 S H H L V L V Y I G R R V L D C G F L *

1561 TAAATCTTCAGTCAAGTCTTATGATGATTGGTTTATTCAGGTGTAGTAGGTTGTAAATC 1620
 * I F S Q V L * * F G L F R C S R L * I
 K S S V K S Y , D D L V Y S G V V G C K S
 L N L Q S S L M M I W F I Q V * * V V N

FIG. 2 CONT.

1621 TATTGTTAAAGAACTGCTCTTATTACTCATGCACTTTACTTAGATTATGTTCAATGTAA 1680
Y C * R N C S Y Y S C T L L R L C S M *
I V K E T A L I T H A L Y L D Y V Q C K
L L L K K L L L L L M H F T * I M F N V

1681 GTGTGGTAATCTTGAACAAATCATATTCTTGGCGTTAATAATTCTTGGTGTAGGCAACT 1740
V W * S * T K S Y S W R * * F L V * A T
C G N L E Q N H I L G V N N S W C R Q L
S V V I L N K I I F L A L I I L G V G N

1741 GTTGCTTAATAGAGGTGATTATAATATGCTTCTAAAAATATTGACTTGTGTTTGTAAAGCG 1800
V A * * R * L * Y A S K K Y * L V C * A
L L N R G D Y N M L L K N I D L F V K R
C C L I E V I I I C F * K I L T C L L S

1801 TCGTGCTGATTTTGCTTGCAAGTTTGCAAGTTTGTGGAGATGGTTTTGTACCTTTTTTACT 1860
S C * F C L Q V C S L W R W F C T F F T
R A D F A C K F A V C G D G F V P F L L
V V L I L L A S L Q F V E M V L Y L F Y

1861 AGATGGTTTAATTCCCGTAGTTATTATCTAATTCAGAGTGGTATTTTCTTTACATCTTT 1920
R W F N S P * L L S N S E W Y F L Y I F
D G L I P R S Y Y L I Q S G I F F T S L
* M V * F P V V I I * F R V V F S L H L

1921 GATGCTCAATTTTCACAAGAAGTTTCTGATATGTGTTTAAAAATGTGTATTTTGTGTTAT 1980
D V S I F T R S F * Y V F K N V Y F V Y
M S Q F S Q E V S D M C L K M C I L F M
* C L N F H K K F L I C V * K C V F C L

1981 GGACAGAGTTTCAGTTGCTACATTTTATATAGAGCATTATGTTAATAGGTTGGTTACTCA 2040
G Q S F S C Y I L Y R A L C * * V G Y S
D R V S V A T F Y I E H Y V N R L V T Q
W T E F Q L L H F I * S I M L I G W L L

2041 ATTTAAGTTATTGGGTACTACCTTGTTAATAAAATGGTTAATGGTTTAAATACCATGTT 2100
I * V I G Y Y T C * * N G * L V * Y H V
F K L L G T T L V N K M V N W F N T M L
N L S Y W V L H L L I K W L I G L I P C

2101 AGATGCTAGTGCACCTGCTACAGGCTGGCTTCTTTACCAATTATTGAATGGTCTTTTTGT 2160
R C * C T C Y R L A S L P I I E W S F C
D A S A P A T G W L L Y Q L L N G L F V
* M L V H L L Q A G F F T N Y * M V F L

FIG. 2 CONT.

2161 AGTATCTCAAGCCAACTTTAATTTTGTGCTTTAATACCTGATTATGCTAAAAATTTAGT 2220
 S I S S Q L * F C C F N T * L C * N F S
 V S Q A N F N F V A L I P D Y A K I L V
 * Y L K P T L I L L L * Y L I M L K F *

2221 TAATAAATTTTACACTTTTAAAGTTATTATTAGAGTGTGTACAGTTGATGTTTAA 2280
 * * I L H F F * V I I R V C Y S * C F K
 N K F Y T F F K L L L E C V T V D V L K
 L I N F T L F L S Y Y * S V L Q L M F *

2281 AGATATGCCTGTTCTTAAACTATTAAATGGTTTAGTTTGTATTGTAGGCAATAAGTTT 2340
 R Y A C S * N Y * W F S L Y C R Q * V L
 D M P V L K T I N G L V C I V G N K F Y
 K I C L F L K L L M V * F V L * A I S F

2341 TAACGTTAGTACAGGGTTAATTCCTGGTTTGTATTTACCATGTAATGCACAGGAACA 2400
 * R * Y R V N S W F C F T M * C T G T T
 N V S T G L I P G F V L P C N A Q E Q Q
 I T L V Q G * F L V L F Y H V M H R N N

2401 AATTTATTTTTTTGAAGGCGTTGCAGAATCTGTTATAGTAGAAGATGATGTTATTGAGAA 2460
 N L F F * R R C R I C Y S R R * C Y * E
 I Y F F E G V A E S V I V E D D V I E N
 K F I F L K A L Q N L L * * K M M L L R

2461 TGTCAAATCTTCTTTATCATCTTATGAGTATTGTCAACCACCTAAATCTGTAGAAAAAAT 2520
 C Q I F F I I L * V L S T T * I C R K N
 V K S S L S S Y E Y C Q P P K S V E K I
 M S N L L Y H L M S I V N H L N L * K K

2521 TTGTATTATAGATAATATGTACATGGGTAAGTGTGGTGATAAATTTTCCCTATTGTAT 2580
 L Y Y R * Y V H G * V W * * I F P Y C H
 C I I D N M Y M G K C G D K F F P I V M
 F V L * I I C T W V S V V I N F S L L S

2581 GAATGATAAAAAATATTGTCTTTTAGATCAGGCTTGGCGTTTCCATGTGCAGGTAGAAA 2640
 E * * K Y L S F R S G L A F S M C R * K
 N D K N I C L L D Q A W R F P C A G R K
 * M I K I F V F * I R L G V F H V Q V E

2641 AGTTAATTTTAACGAGAAACCTGTTGTTATGGAGATTCCGTCTTTGATGACAGTTAAGGT 2700
 S * F * R E T C C Y G D S V F D D S * G
 V N F N E K P V V M E I P S L M T V K V
 K L I L T R N L L L W R F R L * * Q L R

FIG. 2 CONT.

2701 TATGTTTGATTAGATTCTACTTTTGATGATATTTTAGGTAAAGTTTGTTTCTAGAAATTTGA 2760
Y V * F R F Y F * * Y F R * S L F R I *
M F D L D S T F D D I L G K V C S E F E
L C L I * I L L L M I F * V K F V Q N L

2761 AGTAGAAAAGGGTGTTACTGTAGATGATTTTGTGCTGTTGTTTGTGATGCTATAGAGAA 2820
S R K G C Y C R * F C C C C L * C Y R E
V E K G V T V D D F V A V V C D A I E N
K * K R V L L * M I L L L L F V M L * R

2821 TGCTTTAAACTCTTGTAAGAGCATCCAGTGGTTGGTTATCAAGTTCGTGCATTTTAA 2880
C F K L L * R A S S G W L S S S C I F K
A L N S C K E H P V V G Y Q V R A F L N
M L * T L V K S I Q W L V I K F V H F *

2881 TAACTTAATGAGAATGTTGTTTATTTATTTGATGAGGCTGGTGATGAAGCAATGGCCTC 2940
* T * * E C C L F I * * G W * * S N G L
K L N E N V V Y L F D E A G D E A M A S
I N L M R M L F I Y L M R L V M K Q W P

2941 TCGTATGTATGTACTTTTGCTATTGAGGATGTTGAAGACGTTATCAGTAGTGAAGCTGT 3000
S Y V L Y F C Y * G C * R R Y Q * * S C
R M Y C T F A I E D V E D V I S S E A V
L V C I V L L L L R M L K T L S V V K L

3001 CGAAGATACTATTGATGGTGTGTTGAAGACACTATTAATGACGATGAAGATGTTGTTAC 3060
R R Y Y * W C R * R H Y * * R * R C C Y
E D T I D G V V E D T I N D D E D V V T
S K I L L M V S L K T L L M T M K M L L

3061 TGGTGACAATGACGATGAAGATGTTGTTACTGGTGACAATGACGATGAAGATGTTGTTAC 3120
W * Q * R * R C C Y W * Q * R * R C C Y
G D N D D E D V V T G D N D D E D V V T
L V T M T M K M L L L V T M T M K M L L

3121 TGGTGACAATGACGATGAAGATGTTGTTACTGGTGACAATGACGATGAAGATGTTGTTAC 3180
W * Q * R * R C C Y W * Q * R * R C C Y
G D N D D E D V V T G D N D D E D V V T
L V T M T M K M L L L V T M T M K M L L

3181 TGGTGACAATGACGATGAAGATGTTGTTACTGGTGACAATGACGATGAAGATGTTGTTAC 3240
W * Q * R * R C C Y W * Q * R * R C C Y
G D N D D E D V V T G D N D D E D V V T
L V T M T M K M L L L V T M T M K M L L

FIG. 2 CONT.

3241 TGGTGACAATGACGATGAAGATGTTGTTACTGGTGACAATGACGATGAAGATGTTGTTAC 3300
 W * Q * R * R C C Y W * Q * R * R C C Y
 G D N D D E D V V T G D N D D E D V V T
 L V T M T M K M L L L V T M T M K M L L

3301 TGGTGACAATGACGATGAAGATGTTGTTACTGGTGACAATGACGATGAAGATGTTGTTAC 3360
 W * Q * R * R C C Y W * Q * R * R C C Y
 G D N D D E D V V T G D N D D E D V V T
 L V T M T M K M L L L V T M T M K M L L

3361 TGGTGACAATGACGATGAAGATGTTGTTACTGGTGACAATGACGATGAAGATGTTGTTAC 3420
 W * Q * R * R C C Y W * Q * R * R C C Y
 G D N D D E D V V T G D N D D E D V V T
 L V T M T M K M L L L V T M T M K M L L

3421 TGGTGACAATGACGATGAAGATGTTGTTACTGGTGACAATAACGATGAAGAGATTGTTAC 3480
 W * Q * R * R C C Y W * Q * R * R D C Y
 G D N D D E D V V T G D N N D E E I V T
 L V T M T M K M L L L V T I T M K R L L

3481 TGGTGACAATGATGACCAAATTGTTGTTACTGGTGATGATGTAGATGATATTGAAAGTAT 3540
 W * Q * * P N C C Y W * * C R * Y * K Y
 G D N D D Q I V V T G D D V D D I E S I
 L V T M M T K L L L L V M M * M I L K V

3541 TTATGACTTTGATACTTATAAAGCTCTTTTAGTTTTAATGATGCTATAATGATGCTTT 3600
 L * L * Y L * S S F S F * * C L * * C F
 Y D F D T Y K A L L V F N D V Y N D A L
 F M T L I L I K L F * F L M M S I M M L

3601 GTTGTAGTTATGGTTCTAGTGTGAAACAGAAACATATTTTAAAGTTAATGGTTTATG 3660
 V C * L W F * C * N R N I F * S * W F M
 F V S Y G S S V E T E T Y F K V N G L W
 C L L V M V L V L K Q K H I L K L M V Y

3661 GTCACCTACTATTACACATACTAATTGTTGGTTGCGTTCTGTGTTACTTGTAAATGCAGAA 3720
 V T Y Y Y T Y * L L V A F C V T C N A E
 S P T I T H T N C W L R S V L L V M Q K
 G H L L L H I L I V G C V L C Y L * C R

3721 ATTACCTTTTAAAGTTTAAAGGATTAGCTATTGAAAATATGTGGTTATCTTATAAGGTGGG 3780
 I T F * V * G F S Y * K Y V V I L * G G
 L P F K F K D L A I E N M W L S Y K V G
 N Y L L S L R I * L L K I C G Y L I R W

FIG. 2 CONT.

3781 TTATAATCAAAGTTTGTGATTATTTACTGACCACTATTCCTAAAGCTATTGTTTGGCC 3840
L * S K F C * L F T D H Y S * S Y C F A
Y N Q S F V D Y L L T T I P K A I V L P
V I I K V L L I I Y * P L F L K L L F C

3841 TCAAGGTGGTTTTGTAGCTGATTTTGCTTATTGGTTTTTAAACCAGTTTGATATTAATGC 3900
S R W F C S * F C L L V F K P V * Y * C
Q G G F V A D F A Y W F L N Q F D I N A
L K V V L * L I L L I G F * T S L I L M

3901 GTATGCTAATTGGTGTGTTTTAAATGTGGTTTTCTTTTGATTAAATGGTTTGGATGC 3960
V C * L V L F K M W F F F * F K W F G C
Y A N W C C L K C G F S F D L N G L D A
R M L I G V V * N V V F L L I * M V W M

3961 TTTGTTTTTTTATGGAGATATTGTGTCTCATGTTTGTAAAGTGTGGACATAATATGACTCT 4020
F V F L W R Y C V S C L * V W T * Y D S
L F F Y G D I V S H V C K C G H N M T L
L C F F M E I L C L M F V S V D I I * L

4021 AATAGCAGCGGACTTACCTTGTACATTACATTTTTCATTATTTGATGACAATTTTGTGC 4080
N S S G L T L Y I T F F I I * * Q F L C
I A A D L P C T L H F S L F D D N F C A
* * Q R T Y L V H Y I F H Y L M T I F V

4081 TTTTTCACCCCTAAAAAATTTTATTGCTGCATGTGCTGTGGATGTAAACGTTTGTCA 4140
F L H P * K N F Y C C M C C G C K R L S
F C T P K K I F I A A C A V D V N V C H
L F A P L K K F L L L H V L W M * T F V

4141 TTCTGTAGCTGTTATAGGTGATGAACAAATAGATGGTAAGTTTGTACTAAATTTAGTGG 4200
F C S C Y R * * T N R W * V C Y * I * W
S V A V I G D E Q I D G K F V T K F S G
I L * L L * V M N K * M V S L L L N L V

4201 TGATAAATTTGATTTTATAGTAGCTTATGGAATGTCATTTAGTATGTCTTCTTTTGAGTT 4260
* * I * F Y S R L W N V I * Y V F F * V
D K F D F I V G Y G M S F S M S S F E L
V I N L I L * * V M E C H L V C L L L S

4261 ACCTCAATTGTATGGTTTGTGTATAACACCTAATGTATGTTTTGTTAAAGGTGATATTAT 4320
T S I V W F V Y N T * C M F C * R * Y Y
P Q L Y G L C I T P N V C F V K G D I I
Y L N C M V C V * H L M Y V L L K V I L

FIG. 2 CONT.

4321 AAATGTTGCTAGACTTGTAAAGCTGATGTTATTGTTAATCCTGCTAATGGGCATATGCT 4380
K C C * T C * S * C Y C * S C * W A Y A
N V A R L V K A D V I V N P A N G H M L
* M L L D L L K L M L L L I L L M G I C

4381 CCATGGTGGTGGAGTTGCAAAAGCTATAGCTGTAGCTGCAGGTAAAAAATTTCTAAAGA 4440
P W W W S C K S Y S C S C R * K I F * R
H G G G V A K A I A V A A G K K F S K E
S M V V E L Q K L * L * L Q V K N F L K

4441 AACTGCTGCTATGGTTAAATCTAAAGGTGTTGCCAAGTAGGAGATTGTTATGTTTCTAC 4500
N C C Y G * I * R C L P S R R L L C F Y
T A A M V K S K G V C Q V G D C Y V S T
K L L L W L N L K V F A K * E I V M F L

4501 CGGTGGTAAATTATGTAAACAATTCTTAATATTGTAGGCCCTGATGCTAGACAAGATGG 4560
R W * I M * N N S * Y C R P * C * T R W
G G K L C K T I L N I V G P D A R Q D G
P V V N Y V K Q F L I L * A L M L D K M

4561 AAGACAATCTTATGTTTTGTTAGCACGTGCTTATAAGCATCTTAATAATTATGATTGTTG 4620
K T I L C F V S T C L * A S * * L * L L
R Q S Y V L L A R A Y K H L N N Y D C C
E D N L M F C * H V L I S I L I I M I V

4621 TTTGTCTACTCTCATATCGGCTGGTATATTAGTGTTCCTGCTGATGTGTCATTAACCTTA 4680
F V Y S H I G W Y I * C S C * C V I N L
L S T L I S A G I F S V P A D V S L T Y
V C L L S Y R L V Y L V F L L M C H * L

4681 CCTTCTAGGTGTGTTGATAAACAAGTTATCCTTGTAGTAATAATAAAGAAGATTTTGA 4740
P S R C C * * T S Y P C * * * * R R F *
L L G V V D K Q V I L V S N N K E D F D
T F * V L L I N K L S L L V I I K K I L

4741 TATTATTCAAAAATGTCAAATTACTTCAGTTGTTGTTACTAAAGCATTGGCTGTTAGATT 4800
Y Y S K M S N Y F S C W Y * S I G C * I
I I Q K C Q I T S V V G T K A L A V R L
I L F K N V K L L Q L L V L K H W L L D

4801 AACTGCTAATGTAGGCCGTGTTATTAAATTTGAGACAGATGCATACAACTTTTGTGAG 4860
N C * C R P C Y * I * D R C I Q T F F E
T A N V G R V I K F E T D A Y K L F L S
* L L M * A V L L N L R Q M H T N F F *

FIG. 2 CONT.

4861 TGGTGATGATTGTTTTGTTTCAAATTCTTCTGTTATACAAGAAGTTTATTGCTTCGTCA 4920
W * * L F C F K F F C Y T R S F I A S S
G D D C F V S N S S V I Q E V L L L R H
V V M I V L F Q I L L L Y K K F Y C F V

4921 TGATATACAATTGAATAATGACGTCGTGATTATTGTTGTCTAAGATGACTAGTCTTCC 4980
* Y T I E * * R S * L F V V * D D * S S
D I Q L N N D V R D Y L L S K M T S L P
M I Y N * I M T F V I I C C L R * L V F

4981 TAAAGATTGGCGTCTTATCAATAAATTTGATGTTATTAACGGTGTTAAACTGTTAAGTA 5040
* R L A S Y Q * I * C Y * R C * N C * V
K D W R L I N K F D V I N G V K T V K Y
L K I G V L S I N L M L L T V L K L L S

5041 TTTTGAGTGTCTAATTCTATTATATATCTAGTCAGGGTAAAGACTTTGGTTATGTATG 5100
F * V S * F Y L Y M * S G * R L W L C M
F E C P N S I Y I C S Q G K D F G Y V C
I L S V L I L F I Y V V R V K T L V M Y

5101 TGATGGTTCTTTTTATAAAGCAACTGTTAATCAAGTTTGTGTTTTATTAGCTAAGAAGAT 5160
* W F F L * S N C * S S L C F I S * E D
D G S F Y K A T V N Q V C V L L A K K I
V M V L F I K Q L L I K F V F Y * L R R

5161 AGATGTTTTGCTTACTGTAGATGGTGTAAATTTTAAATCTATTCTCTTACTGTAGGTGA 5220
R C F A Y C R W C * F * I Y F S Y C R *
D V L L T V D G V N F K S I S L T V G E
* M F C L L * M V L I L N L F L L L * V

5221 AGTTTTTGGTAAATACTTGGTAATGTTTTCTGTGATGGCATTGATGTTACTAAGTTAAA 5280
S F W * N T W * C F L * W H * C Y * V K
V F G K I L G N V F C D G I D V T K L K
K F L V K Y L V M F S V M A L M L L S *

5281 GTGTAGTGATTTTTATGCCGATAAAATTTATATCAGTATGAAAATTTGTCTTTAGCTGA 5340
V * * F L C R * N F I S V * K F V F S *
C S D F Y A D K I L Y Q Y E N L S L A D
S V V I F M P I K F Y I S M K I C L * L

5341 TATTTCTGCTGTACAAAGTTCATTGGGTTTGATCAGCAACAATTGCTTGCTTATTATAA 5400
Y F C C T K F I W V * S A T I A C L L *
I S A V Q S S F G F D Q Q Q L L A Y Y N
I F L L Y K V H L G L I S N N C L L I I

FIG. 2 CONT.

5401 TTTTAAACAGTATGTAAATGGTCTGTAGTTGTTAACGGTCCATTTTTCTTTGAACA 5460
 F F N S M * M V C S C * R S I F F F * T
 F L T V C K W S V V V N G P F F S F E Q
 I F * Q Y V N G L * L L T V H F F L L N

5461 GTCTCATAATAATTGTTATGTGAATGTAGCTTGTCTTATGTTGCAGCATATTAATCTTAA 5520
 V S * * L L C E C S L S Y V A A Y * S *
 S H N N C Y V N V A C L M L Q H I N L K
 S L I I I V M * M * L V L C C S I L I L

5521 ATTTAATAAATGGCAGTGGCAGGAAGCATGGTATGAATTCGTGCTGGCAGACCACATAG 5580
 I * * M A V A G S M V * I S C W Q T T *
 F N K W Q W Q E A W Y E F R A G R P H R
 N L I N G S G R K H G M N F V L A D H I

5581 GTTAGTGTCTCTTGTTTTAGCTAAAGGTCATTTTAAATTTGATGAACCATCAGATGCTAC 5640
 V S C S C F S * R S F * I * * T I R C Y
 L V A L V L A K G H F K F D E P S D A T
 G * L L L F * L K V I L N L M N H Q M L

5641 TGATTTTATTCGTGTGTGTTTGAACAAGCTGATTTATCAGGTGCAATTTGTGAATTAGA 5700
 * F Y S C C F E T S * F I R C N L * I R
 D F I R V V L K Q A D L S G A I C E L E
 L I L F V L F * N K L I Y Q V Q F V N *

5701 ACTTATTTGTGATTGTGGTATTAAACAAGAAAGTCGTGTGGTGTGATGCTGTTATGCA 5760
 T Y L * L W Y * T R K S C W C * C C Y A
 L I C D C G I K Q E S R V G V D A V M H
 N L F V I V V L N K K V V L V L M L L C

5761 TTTTGGTACATTAGCAAAGACTGATCTTTTAAATGGTTATAAGATTGGCTGTAATTGTGC 5820
 F W Y I S K D * S F * W L * D W L * L C
 F G T L A K T D L F N G Y K I G C N C A
 I L V H * Q R L I F L M V I R L A V I V

5821 AGGTAGAATTGTCCATTGTACTAAATTGAATGTACCATTTTGTATTGTTCTAATACTCC 5880
 R * N C P L Y * I E C T I F D L F * Y S
 G R I V H C T K L N V P F L I C S N T P
 Q V E L S I V L N * M Y H F * F V L I L

5881 TCTGAGTAAGGATTTACCTGATGATGTTGTTGCAGCTAACATGTTTATGGGTGTAGGTGT 5940
 S E * G F T * * C C C S * H V Y G C R C
 L S K D L P D D V V A A N M F M G V G V
 L * V R I Y L M M L L Q L T C L W V * V

FIG. 2 CONT.

5941 AGGCCATTATACACATTTGAAATGTGGTTCACCTTACCAACATTATGATGCTTGTAGTGT 6000
R P L Y T F E M W F T L P T L * C L * C
G H Y T H L K C G S P Y Q H Y D A C S V
* A I I H I * N V V H L T N I M M L V V

6001 TAAAAAATATACAGGTGTTAGTGGTGTGTTAACTGACTGCTTGTATCTTAAAAATTTAAC 6060
* K I Y R C * W L F N * L L V S * K F N
K K Y T G V S G C L T D C L Y L K N L T
L K N I Q V L V V V * L T A C I L K I *

6061 CCAGACTTTTACATCTATGTTGACTAATTATTTTTGGATGATGTTGAAATGGTTGCTTA 6120
P D F Y I Y V D * L F F G * C * N G C L
Q T F T S M L T N Y F L D D V E M V A Y
P R L L H L C * L I I F W M M L K W L L

6121 TAACCCTGATCTTTCACAATATTATTGTGATAATGGTAAGTATTATACAAAACCTATTAT 6180
* P * S F T I L L * * W * V L Y K T Y Y
N P D L S Q Y Y C D N G K Y Y T K P I I
I T L I F H N I I V I M V S I I Q N L L

6181 AAAGGCTCAGTTTAAACCATTGCTAAAGTTGACGGTGTGTTATACTAACTTTAAGTTAGT 6240
K G S V * T I C * S * R C L Y * L * V S
K A Q F K P F A K V D G V Y T N F K L V
* R L S L N H L L K L T V F I L T L S *

6241 TGGACATGATATTTGTGCTCAATTGAATGATAAGTTAGGTTTTAATGTAGATTGCCGTT 6300
W T * Y L C S I E * * V R F * C R F A V
G H D I C A Q L N D K L G F N V D L P F
L D M I F V L N * M I S * V L M * I C R

6301 TGTGAGTACAAAGTAACAGTCTGGCCTGTAGCTACTGGTGATGTTGTTTTGGCATCTGA 6360
C * V Q S N S L A C S Y W * C C F G I *
V E Y K V T V W P V A T G D V V L A S D
L L S T K * Q S G L * L L V M L F W H L

6361 TGATTTATATGTGAAACGTTATTTTAAAGGATGTGAAACTTTTGGTAAGCCTGTTATTTG 6420
* F I C E T L F * R M * N F W * A C Y L
D L Y V K R Y F K G C E T F G K P V I W
M I Y M * N V I L K D V K L L V S L L F

6421 GTTTTGTGATGATGAAGCATCATTGAATTCTTACTTATTTTAATAAACCTAGTTTAA 6480
V L S * * S I I E F S Y L F * * T * F *
F C H D E A S L N S L T Y F N K P S F K
G F V M M K H H * I L L L I L I N L V L

FIG. 2 CONT.

6481 ATCTGAAAAATAGATATAGTGTGTTTGTCTGTTGATTCTGTATCTGAGGAGTCACAAGGTAA 6540
I * K * I * C F V C * F C I * G V T R *
S E N R Y S V L S V D S V S E E S Q G N
N L K I D I V F C L L I L Y L R S H K V

6541 TGTGGTTACTTCTGTTATGGAATCGCAGATTAGTACTAAAGAGGTTAAGTTAAAGGGTGT 6600
C G Y F C Y G I A D * Y * R G * V K G C
V V T S V M E S Q I S T K E V K L K G V
M W L L L L W N R R L V L K R L S * R V

6601 TAGAAAGACTGTAAATAGAAGATGCTATTATTGTTAATGATGAAAAATAGTTCTATTAA 6660
* K D C * N R R C Y Y C * * * K * F Y *
R K T V K I E D A I I V N D E N S S I K
L E R L L K * K M L L L L M M K I V L L

6661 GGTGTGTTAAAGTTTATCTTTAGTTGATGTTTGGGATATGTATTTGACAGGTTGTGATTA 6720
G C * K F I F S * C L G Y V F D R L * L
V V K S L S L V D V W D M Y L T G C D Y
R L L K V Y L * L M F G I C I * Q V V I

6721 TGTGTTTGGGTTGCTAATGAATTGTCACGCCTAGTTAAATCACCAACAGTTAGGGAATA 6780
C C L G C * * I V T P S * I T N S * G I
V V W V A N E L S R L V K S P T V R E Y
M L F G L L M N C H A * L N H Q Q L G N

6781 TATACGATATGGTATTAAACCTATTACTATACCTATAGATTGTTATGTTTAAGAGATGA 6840
Y T I W Y * T Y Y Y T Y R F V M F K R *
I R Y G I K P I T I P I D L L C L R D D
I Y D M V L N L L L Y L * I C Y V * E M

6841 TAATCAAACCTCTTTTAGTTCCTAAAATTTTAAAGCAAGAGCTATAGAATTTTATGGTTT 6900
* S N S F S S * N F * S K S Y R I L W F
N Q T L L V P K I F K A R A I E F Y G F
I I K L F * F L K F L K Q E L * N F M V

6901 TTTGAAGTGGTTGTTTATTTATGTTTTAGTTTATTACATTTTACAAATGATAAAACCAT 6960
F E V V V Y L C F * F I T F Y K * * N H
L K W L F I Y V F S L L H F T N D K T I
F * S G C L F M F L V Y Y I L Q M I K P

6961 TTTTATACTACAGAAATAGCTTCTAAGTTTACTTTTAATTTGTTTTGTTGGCTCTTAA 7020
F L Y Y R N S F * V Y F * F V L F G S *
F Y T T E I A S K F T F N L F C L A L K
F F I L Q K * L L S L L L I C F V W L L

FIG. 2 CONT.

7021 AAATGCTTTTCAGACATTAGATGGAGTATATTTATAAAAGGTTTCTTGTTGTAGCCAC 7080
K C F S D I * M E Y I Y K R F S C C S H
N A F Q T F R W S I F I K G F L V V A T
K M L F R H L D G V Y L * K V F L L * P

7081 TGTGTTTTTGTGTTTGGTTTAATTTTTGTATATAAAATGTTATTTTGTAGTACTTTTATCT 7140
C V F V L V * F F V Y K C Y F * * L L S
V F L F W F N F L Y I N V I F S D F Y L
L C F C F G L I F C I * M L F L V T F I

7141 TCCTAATATTAGTGTGTTTTCCTATTTTGTGGGAAGAATGTTATGTGGATAAAGGCTAC 7200
S * Y * C F S Y F C G K N C Y V D K G Y
P N I S V F P I F V G R I V M W I K A T
F L I L V F F L F L W E E L L C G * R L

7201 TTTTGGTTTGGTTACAATTTGTGATTTTATTCTAAGTTAGGTGTAGGTTTACAAGTCA 7260
F W F G Y N L * F L F * V R C R F Y K S
F G L V T I C D F Y S K L G V G F T S H
L L V W L Q F V I F I L S * V * V L Q V

7261 TTTTTGTAATGCTAGTTTATATGTGAATTGTGTCATTCTGTTTTGATATGTTGCATAC 7320
F L * W * F Y M * I V S F W F * Y V G Y
F C N G S F I C E L C H S G F D M L D T
I F V M V V L Y V N C V I L V L I C W I

7321 ATATGCAGCTATAGATTTTGTTCAGTATGAAGTAGATAGACGTGTTTTATTGATTATGT 7380
I C S Y R F C S V * S R * T C F I * L C
Y A A I D F V Q Y E V D R R V L F D Y V
H M Q L * I L F S M K * I D V F Y L I M

7381 TAGTTTAGTCAAATTAATTGTTGAACTCGTTATTGGTTATTTCATTATACACAGTATGTT 7440
* F S Q I N C * T R Y W L F I I H S M V
S L V K L I V E L V I G Y S L Y T V W F
L V * S N * L L N S L L V I H Y T Q Y G

7441 TTATCCATTATTTGTCTTATTGTTTACAATTATTTACTACATGGTTGCCTGATTGTT 7500
L S I I L S Y W F T I I Y Y M V A * F V
Y P L F C L I G L Q L F T T W L P D L F
F I H Y F V L L V Y N Y L L H G C L I C

7501 TATGTTAGAACTATGCATTGTTGATTAGATTTATTGTATTTGTAGCTAATATGTTACC 7560
Y V R N Y A L V D * I Y C I C S * Y V T
M L E T M H W L I R F I V F V A N M L P
L C * K L C I G * L D L L Y L * L I C Y

FIG. 2 CONT.

7561 TGCTTTTGTCTTGTGCGGTTTTATATAGTTGTTACTGCTATGTATAAAGTAGTTGGTTT 7620
C F C L V A V L Y S C Y C Y V * S S W F
A F V L L R F Y I V V T A M Y K V V G F
L L L S C C G F I * L L L L C I K * L V

7621 TATTAGGCATATTGTCTATGGTTGTAATAAAGCTGGTTGTTTATTTTGTATAAACGAAA 7680
Y * A Y C L W L * * S W L F I L L * T K
I R H I V Y G C N K A G C L F C Y K R N
L L G I L S M V V I K L V V Y F V I N E

7681 TTGTAGTGTTTCGTGTTAAGTGTAGTACTATTGTTGGTGGTGAATTCGTTATTATGATAT 7740
L * C S C * V * Y Y C W W C N S L L * Y
C S V R V K C S T I V G G V I R Y Y D I
I V V F V L S V V L L L V V * F V I M I

7741 TACTGCTAATGGTGGTACTGGTTTTCTGTTAAACATCAATGGAATTGTTTAAATGCCA 7800
Y C * W W Y W F L C * T S M E L F * L P
T A N G G T G F C V K H Q W N C F N C H
L L L M V V L V F V L N I N G I V L I A

7801 TTCTTTTAAACCAGGTAACACTTTTTATACTGTAGAAGCTGCTATAGAAGTTTCTAAAGA 7860
F F * T R * H F Y N C R S C Y R T F * R
S F K P G N T F I T V E A A I E L S K E
I L L N Q V T L L * L * K L L * N F L K

7861 GCTTAAACGACCTGTAAATCCAACCTGATGCTTCACATTATGTAGTTACTGATATTAAGCA 7920
A * T T C K S N * C F T L C S Y * Y * A
L K R P V N P T D A S H Y V V T D I K Q
S L N D L * I Q L M L H I M * L L I L S

7921 AGTTGGTTGTATGATGCGTTTGTCTATGATAGAGATGGACAGCGTGTTTACGATGATGT 7980
S W L Y D A F V L * * R W T A C L R * C
V G C M M R L F Y D R D G Q R V Y D D V
X L V V * C V C S M I E M D S V F T M M

7981 TGATGCTAGTTTATTTGTAGATATTAATAATCTGTTACATTCTAAAGTTAAAGTTGTTCC 8040
* C * F I C R Y * * S V T F * S * S C S
D A S L F V D I N N L L H S K V K V V P
L M L V Y L * I L I I C Y I L K L K L F

8041 TAATTTGTATGTAGTTGTAGTAGAGAGTGTGCTGATAGAGCTAATTTTCTGAATGCTGT 8100
* F V C S C S R E * C * * S * F S E C C
N L Y V V V V E S D A D R A N F L N A V
L I C M * L * * R V M L I E L I F * M L

FIG. 2 CONT.

8101 TGTGTTTTATGCACAATCATTGTATAGGCCTATATTACTTGTAGACAAAAAGTTAATTAC 8160
C V L C T I I V * A Y I T C R Q K V N Y
V F Y A Q S L Y R P I L L V D K K L I T
L C F M H N H C I G L Y Y L * T K S * L

8161 TACAGCTTGTAAATGGTATCTCTGTAACCCAGACTATGTTTGATGTTTATGTTGATACTTT 8220
Y S L * W Y L C N P D Y V * C L C * Y F
T A C N G I S V T Q T M F D V Y V D T F
L Q L V M V S L * P R L C L M F M L I L

8221 TATGTCTCATTTTIGATGTTGATAGAAAGAGTTTAAATAATTTTGTAAACATTGCTCATGC 8280
Y V S F * C * * K E F * * F C * H C S C
M S H F D V D R K S F N N F V N I A H A
L C L I L M L I E R V L I I L L T L L M

8281 TTCTCTTAGAGAGGGTGTGCAATTAGAAAAGGTTTATAGATACTTTTGTGGGATGTGTACG 8340
F S * R G C A I R K G F R Y F C G M C T
S L R E G V Q L E K V L D T F V G C V R
L L L E R V C N * K R F * I L L W D V Y

8341 TAAATGTTGTTCCATTGATTCAGATGTTGAAACAAGATTTATTACTAAATCTATGATATC 8400
* M L F H * F R C * N K I Y Y * I Y D I
K C C S I D S D V E T R F I T K S M I S
V N V V P L I Q M L K Q D L L L N L * Y

8401 TGCAGTAGCTGCTGGTTTGAATTTACTGATGAAAATTATAACAATTTGGTACCTACATA 8460
C S S C W F G I Y * * K L * Q F G T Y I
A V A A G L E F T D E N Y N N L V P T Y
L Q * L L V W N L L M K I I T I W Y L H

8461 TTTAAAGAGTGATAATATTGTAGCTGCTGATTAGGTGTTCTTATACAGAATGGTGCTAA 8520
F K E * * Y C S C * F R C S Y T E W C *
L K S D N I V A A D L G V L I Q N G A K
I * R V I I L * L L I * V F L Y R M V L

8521 GCATGTACAGGGTAATGTTGCTAAGGCAGCTAATATTCTTGTATATGGTTTATTGATGC 8580
A C T G * C C * G S * Y F L Y M V Y * C
H V Q G N V A K A A N I S C I W F I D A
S M Y R V M L L R Q L I F L V Y G L L M

8581 TTTTAATCAACTTACTGCTGATTACAGCATAAATTAATAAGCATGTGTAAACTGG 8640
F * S T Y C * F T A * I K K S M C * N W
F N Q L T A D L Q H K L K K A C V K T G
L L I N L L L I Y S I N * K K H V L K L

FIG. 2 CONT.

8641 CTTGAAGTTAAAATTGACTTTTAATAAGCAAGAGGCAAGTGTCCCTATTCTTACAACACC 8700
L E V K I D F * * A R G K C P Y S Y N T
L K L K L T F N K Q E A S V P I L T T P
A * S * N * L L I S K R Q V S L F L Q H

8701 CTTTTCACCTTAAAGGAGGTGTGTATTGAGTAATTTGTTATATATATTATTTTTTGTAG 8760
L F T * R R C C I E * F V I Y I I F C *
F S L K G G V V L S N L L Y I L F F V S
P F H L K E V L Y * V I C Y I Y Y F L L

8761 TTTAATCTGTTTATATTATTGTGGGCTTTATTGCCTACATATAGTGTTTATAAGTCTGA 8820
F N L F Y I I V G F I A Y I * C L * V *
L I C F I L L W A L L P T Y S V Y K S D
V * S V L Y Y C G L Y C L H I V F I S L

8821 TATTCATTTGCCTGCTTATGCTAGTTTTAAAGTTATTGATAATGGTGTGTTAGAGATAT 8880
Y S F A C L C * F * S Y * * W C C * R Y
I H L P A Y A S F K V I D N G V V R D I
I F I C L L M L V L K L L I M V L L E I

8881 TTCAGTTAATGATTTATGTTTTGCTAATAAAATTTTCCAATTTGATCAATGGTATGAGTC 8940
F S * * F M F C * * I F P I * S M V * V
S V N D L C F A N K F F Q F D Q W Y E S
F Q L M I Y V L L I N F S N L I N G M S

8941 CACTTTTGGGTCTGTTTACTATCATAATCTATGGATTGCCCTATTGTAGTGGCAGTTAT 9000
H F W V C L L S * F Y G L P Y C S G S Y
T F G S V Y Y H N S M D C P I V V A V M
P L L G L F T I I I L W I A L L * W Q L

9001 GGATGAAGATATCGGTTCTACTATGTTTAATGTTCTACTAAAGTTTGGAGACATGGCTT 9060
G * R Y R F Y Y V * C S Y * S F E T W L
D E D I G S T M F N V P T K V L R H G F
W M K I S V L L C L M F L L K F * D M A

9061 TCATGTTTACATTTTAACTTATGCATTTGCTAGTGATAGTGTTCAGTGCTATACACC 9120
S C F T F F N L C I C * * * C S V L Y T
H V L H F L T Y A F A S D S V Q C Y T P
F M F Y I F * L M H L L V I V F S A I H

9121 ACATATTCAGATTTCTTATAATGATTTTATGCTAGTGGTGTGTTTATCATCTTTGTG 9180
T Y S D F L * * F L C * W L C F I I F V
H I Q I S Y N D F Y A S G C V L S S L C
H I F R F L I M I F M L V V V F Y H L C

FIG. 2 CONT.

9181 TACTATGTTTAAAAGAGGTGATGGTACACCACATCCTTATTGTTATTTCAGATGGTGTAT 9240
 Y Y V * K R * W Y T T S L L L F R W C Y
 T M F K R G D G T P H P Y C Y S D G V M
 V L C L K E V M V H H I L I V I Q M V L

9241 GAAGAATGCTTCTTTGTATACATCTTTGGTTCCACATACACGTTATAGCCTTGCTAATTC 9300
 E E C F F V Y I F G S T Y T L * P C * F
 K N A S L Y T S L V P H T R Y S L A N S
 * R M L L C I H L W F H I H V I A L L I

9301 TAATGGTTTTATAAGATTTCCTGATGTTATTAGTGAAGGTATTGTACGTATTGTAAGAAC 9360
 * W F Y K I S * C Y * * R Y C T Y C K N
 N G F I R F P D V I S E G I V R I V R T
 L M V L * D F L M L L V K V L Y V L * E

9361 GCGCTCTATGACTTATTGTAGAGTGGGTGCATGTGAATACGCCGAAGAGGGTATATGTTT 9420
 A L Y D L L * S G C M * I R R R G Y M F
 R S M T Y C R V G A C E Y A E E G I C F
 R A L * L I V E W V H V N T P K R V Y V

9421 TAATTTAATAGTTCCTGGGTTTTGAATAATGATTATTATAGAAGTATGCCTGGAACTTT 9480
 * F * * F L G F E * * L L * K Y A W N F
 N F N S S W V L N N D Y Y R S M P G T F
 L I L I V P G F * I M I I I E V C L E L

9481 TTGTGGTAGAGATCTTTTTGATTGTTTTATCAATTTTTTAGTAGTTTAATTCGTCCTAT 9540
 L W * R S F * F V L S I F * * F N S S Y
 C G R D L F D L F Y Q F F S S L I R P I
 F V V E I F L I C F I N F L V V * F V L

9541 AGATTCTCTTTCTCTACTGCTAGTCTATTTTTGGAGCTATATTGGCTATAGTTGTTGT 9600
 R F L F S Y C * F Y F W S Y I G Y S C C
 D F F S L T A S S I F G A I L A I V V V
 * I S F L L L L V L F L E L Y W L * L L

9601 CTTGGTTTTTTATTATTATAAACTTAAGCGTGCTTTTGGAGATTATACTAGTGTGT 9660
 L G F L L F N K T * A C F W R L Y * C C
 L V F Y Y L I K L K R A F G D Y T S V V
 S W F F I I * * N L S V L L E I I L V L

9661 AGTTATAAATGTTGTTGTTTGGTGTATTAATTTCTTATGCTTTTTGTTTTTCAAGTTTA 9720
 S Y K C C C L V Y * F S Y A F C F S S L
 V I N V V V W C I N F L M L F V F Q V Y
 * L * M L L F G V L I F L C F L F F K F

FIG. 2 CONT.

9721 TCCTATTTGTGCATGTGTTTATGCTTGTTTTATTTTATGTAACATTGTATTTTCCTTC 9780
S Y L C M C L C L F L F L C N I V F S F
P I C A C V Y A C F Y F Y V T L Y P P S
I L F V H V F M L V F I F M * H C I F L

9781 TGAAATTAGTGTAATTATGCATTGCAATGGATTGTTATGTATGGTGCTATAATGCCTTT 9840
* N * C N Y A F A M D C Y V W C Y N A F
E I S V I M H L Q W I V M Y G A I M P F
L K L V * L C I C N G L L C M V L * C L

9841 TTGGTTTTGTGTCACATATGTAGCTATGGTTATTGCAAACCATGTTTTATGGTTATTTTC 9900
L V L C H I C S Y G Y C K P C F M V I F
W F C V T Y V A M V I A N H V L W L F S
F G F V S H M * L W L L Q T M F Y G Y F

9901 ATATTGTAGGAAAATTGGTGTTAATGTATGTAGTGATAGTACATTGAAGAAACATCTCT 9960
I L * E N W C * C M * * * Y I * R N I S
Y C R K I G V N V C S D S T F E E T S L
H I V G K L V L M Y V V I V H L K K H L

9961 TACTACTTTTATGATTACTAAAGATTCTTATTGTAGATTAAAGAATTCTGTTTCTGATGT 10020
Y Y F Y D Y * R F L L * I K E F C F * C
T T F M I T K D S Y C R L K N S V S D V
L L L L * L L K I L I V D * R I L F L M

10021 TGCCTACAATAGATATTTGAGTTTGTATAATAAGTATCGTTACTATAGTGGTAAATGGA 10080
C L Q * I F E F V * * V S L L * W * N G
A Y N R Y L S L Y N K Y R Y Y S G K M D
L P T I D I * V C I I S I V T I V V K W

10081 TACTGCTGCCTATAGAGAAGCGCGTGTCTCAGTTAGCTAAAGCTATGGAAACATTTAA 10140
Y C C L * R S G V F S V S * S Y G N I *
T A A Y R E A A C S Q L A K A M E T F N
I L L P I E K R R V L S * L K L W K H L

10141 TCACAATAATGGTAATGATGTCTTATACCAACCTCCTACAGCATCTGTTTCTACATCTTT 10200
S Q * W * * C L I P T S Y S I C F Y I F
H N N G N D V L Y Q P P T A S V S T S F
I T I M V M M S Y T N L L Q H L F L H L

10201 TTTGCAATCAGGTATTGTAAAGATGSTATCTCCTACGTCAAAAATTGAACCTTGTTATTGT 10260
F A I R Y C K D G I S Y V K N * T L Y C
L Q S G I V K M V S P T S K I E P C I V
F C N Q V L * R W Y L L R Q K L N L V L

FIG. 2 CONT.

10261 TAGTGTTACTTATGGTAGTATGACTTTGAATGTTTATGGTTAGATGACAAAGTTTATTG 10320
 * C Y L W * Y D F E W F M V R * Q S L L
 S V T Y G S M T L N G L W L D D K V Y C
 L V L L M V V * L * M V Y G * M T K F I

10321 TCCTCGTCATGTTATATGTTTCATCCTCTAATATGAACGAACCTGATTATTCTGCCTTATT 10380
 S S S C Y M F I L * Y E R T * L F C L I
 P R H V I C S S S N M N E P D Y S A L L
 V L V M L Y V H P L I * T N L I I L P Y

10381 GTGTAGAGTTACTCTAGGTGATTTTACTATAATGTCTGGTCGGATGAGTTTAAACAGTTGT 10440
 V * S Y S R * F Y Y N V W S D E F N S C
 C R V T L G D F T I M S G R M S L T V V
 C V E L L * V I L L * C L V G * V * Q L

10441 GTCTTACCAGATGCAGGGCTGTCAACTGTTTGTGACAGTCTCTTTACAAAATCCTTACAC 10500
 V L P D A G L S T C F D S L F T K S L H
 S Y Q M Q G C Q L V L T V S L Q N P Y T
 C L T R C R A V N L F * Q S L Y K I L T

10501 TCCAAAATATACTTTTGGTAATGTTAAACCTGGTGAACTTTTACTGTTTTAGCTGCGTAA 10560
 S K I Y F W * C * T W * N F Y C F S C V
 P K Y T F G N V K P G E T F T V L A A Y
 L Q N I L L V M L N L V K L L L F * L R

10561 TAATGGCCGACCACAAGGGGCATTTTCATGTTACTATGCGTAGTAGTTATACTATTAAAGG 10620
 * W P T T R G I S C Y Y A * * L Y Y * R
 N G R P Q G A F H V T M R S S Y T I K G
 I M A D H K G H F M L L C V V V I L L K

10621 TTCTTTTTTGTGTGGGTCATGTGGATCTGTTGGTTATGTATTAACAGGTGATAGTGTAA 10680
 F F F V W V M W I C W L C I N R * * C *
 S F L C G S C G S V G Y V L T G D S V K
 V L F C V G H V D L L V M Y * Q V I V L

10681 GTTTGTATATATGCATCAATTAGAGCTCAGTACTGGTTGTACACTGGCACTGATTTTAC 10740
 V C I Y A S I R A Q Y W L S H W H * F Y
 F V Y M H Q L E L S T G C H T G T D F T
 S L Y I C I N * S S V L V V T L A L I L

10741 TGGTAATTTTTATGGTCCATATAGAGATGCTCAAGTTGTACAGTTGCCAGTTAAGGACTA 10800
 W * F L W S I * R C S S C T V A S * G L
 G N F Y G P Y R D A Q V V Q L P V K D Y
 L V I F M V H I E M L K L Y S C Q L R T

FIG. 2 CONT.

10801 CGTCCAGACTGTTAATGTTATTGCTTGGCTCTATGCAGCTATACTTAATAATTGTGCTTG 10860
R P D C * C Y C L A L C S Y T * * L C L
V Q T V N V I A W L Y A A I L N N C A W
T S R L L M L L L G S M Q L Y L I I V L

10861 GTTGTACAAAATGATGTTTGTCTACTGAAGATTTTAAATGTTGGGCTATGGCAAATGG 10920
V C T K * C L F Y * R F * C L G Y G K W
F V Q N D V C S T E D F N V W A M A N G
G L Y K M M F V L L K I L M F G L W Q M

10921 TTTTAGCCAAGTAAAAGCAGATCTTGTCTTAGATGCTTTGGCTTCAATGACAGGTGTTTC 10980
F * P S K S R S C L R C F G F N D R C F
F S Q V K A D L V L D A L A S M T G V S
V L A K * K Q I L S * M L W L Q * Q V F

10981 TATTGAACTTTATTGGCTGCTATTAAGCGTCTATATATGGGATTTCAAGGTCGTCAAAT 11040
Y * N F I G C Y * A S I Y G I S R S S N
I E T L L A A I K R L Y M G F Q G R Q I
L L K L Y W L L L S V Y I W D F K V V K

11041 ACTAGGAAGTTGTACTTTTGAAGATGAATTGGCACCTTCTGACGTTTATCAACAATTGGC 11100
T R K L Y F * R * I G T F * R L S T I G
L G S C T F E D E L A P S D V Y Q Q L A
Y * E V V L L K M N W H L L T F I N N W

11101 TGGTGTAAATGCAATCTAAAACAAAAGATTATTAAAGAAACAATTTATTGGATTTT 11160
W C * I A I * N K K I Y * R N N L L D F
G V K L Q S K T K R F I K E T I Y W I L
L V L N C N L K Q K D L L K K Q F I G F

11161 GATATCTACATTTTGTGTTAGTTGTATAATTTCTGCATTTGTTAAATGGACTATATTTAT 11220
D I Y I F V * L Y N F C I C * M D Y I Y
I S T F L F S C I I S A F V K W T I F M
* Y L H F C L V V * F L H L L N G L Y L

11221 GTATATTAATACACATATGATTGGTGTACATTATGTGTACTTTGTTTTGTTAGTTTTAT 11280
V Y * Y T Y D W C Y I M C T L F C * F Y
Y I N T H M I G V T L C V L C F V S F M
C I L I H I * L V L H Y V Y F V L L V L

11281 GATGTTACTAGTTAAACATAAGCATTTTATTGACTATGTATATAATTCCTGTACTCTG 11340
D V T S * T * A F L F D Y V Y N S C T L
M L L V K H K H F Y L T M Y I I P V L C
* C Y * L N I S I F I * L C I * F L Y S

FIG. 2 CONT.

11341 TACCTTGTTTTATGTAAATTATTTAGTTGTTTATAAGGAAGGTTTATAGAGGTTTACTTA 11400
Y L V L C K L F S C L * G R F * R F Y L
T L F Y V N Y L V V Y K E G F R G F T Y
V P C F M * I I * L F I R K V L E V L L

11401 TGCTGGCTCTCATATTTTGTTCCTGCTGTGAATTTTACTTATGTTTATGAAGTATTTTA 11460
C L A L I F C S C C E F Y L C L * S I L
V W L S Y F V P A V N F T Y V Y E V F Y
M S G S H I L F L L * I L L M F M K Y F

11461 TGGTTGTATTTTATGTGTTTTTGCTATTTTTATAACTATGCATAGTATTAATCATGACAT 11520
W L Y F M C F C Y F Y N Y A * Y * S * H
G C I L C V F A I F I T M H S I N H D I
M V V F Y V F L L F L * L C I V L I M T

11521 TTTTTCTTTGATGTTTTTGTTGGTGAAGATGTTACTTTAATTTCTATGTGGTATTTTGG 11580
F F F D V F G W * N S Y F N F Y V V F W
F S L M F L V G R I V T L I S M W Y F G
F F L * C F W L V E * L L * F L C G I L

11581 GTCGAATTTAGAAGAGGATGTTTTGTTATTTATTACAGCCTTTTATAGTACTTATACATG 11640
V E F R R G C F V I Y Y S L F R Y L Y M
S N L E E D V L L F I T A F L G T Y T W
G R I * K R M F C Y L L Q P F * V L I H

11641 GACCACTATTTGTCTATTAGCTATAGCAAAAATTGTTGCTAATTGGTTGCTCTGTTAATAT 11700
D H Y F V I S Y S K N C C * L V V C * Y
T T I L S L A I A K I V A N W L S V N I
G P L F C H * L * Q K L L L I G C L L I

11701 ATTTTATTTTACAGATGTACCTTATATTAAATTGATTCTCTTGAGTTACTTATTTATAGG 11760
I L F Y R C T L Y * I D S L E L L I Y R
F Y F T D V P Y I K L I L L S Y L F I G
Y F I L Q M Y L I L N * F S * V T Y L *

11761 GTATATTTTATCTTGTATTGTTGGGATTTTTCTCTCTTTTAAACAGTGTTTTATAGAATGCC 11820
V Y F I L L L G I F L S F K Q C F * N A
Y I L S C Y W G F F S L L N S V F R M P
G I F Y L V I G D F S L F * T V F L E C

11821 TATGGGTGTTTATAATTATAAAAATTCTGTTCAAGAATTGCGTTATATGAATGCTAATGG 11880
Y G C L * L * N F C S R I A L Y E C * W
M G V Y N Y K I S V Q E L R Y M N A N G
L W V F I I I K F L F K N C V I * M L M

FIG. 2 CONT.

11881 CTTACGTCCACCTCGTAATAGTTTTTGAGGCTATTTTGTAAATTAAAACTGCTTGAAT 11940
 L T S T S * * F * G Y F V K F K T A W N
 L R P P R N S F E A I L L N L K L L G I
 A Y V H L V I V L R L F C * I * N C L E

11941 AGGTGGCGTGCCAGTTATTGAAGTCTCCCAAATTCATCAAAATTGACTGATGTGAAATG 12000
 R W R A S Y * S L P N S I K I D * C E M
 G G V P V I E V S Q I Q S K L T D V K C
 * V A C Q L L K S P K F N Q N * L M * N

12001 TGCTAATGTTGTTTTGTAAATTGTTTACAGCATTTCATGTTGCTTCTAATTCTAAGTT 12060
 C * C C F V K L F T A F A C C F * F * V
 A N V V L L N C L Q H L H V A S N S K L
 V L M L F C * I V Y S I C M L L L I L S

12061 GTGGCAGTATTGTAGTGTTTTACATAATGAAATACTATCTACTTCAGATTTGAGTGTAGC 12120
 V A V L * C F T * * N T I Y F R F E C S
 W Q Y C S V L H N E I L S T S D L S V A
 C G S I V V F Y I M K Y Y L L Q I * V *

12121 TTTTGATAAGCTTGCTCAATTATTGATTGTTTTATTGCGCAATCCTGCTGCAGTTGATAC 12180
 F * * A C S I I D C F I R Q S C C S * Y
 F D K L A Q L L I V L F A N P A A V D T
 L L I S L L N Y * L F Y S P I L L Q L I

12181 TAAGTGTCTTGCAAGTATAGATGAAGTTAGCGATGATTATGTTCAAGATAGTACCGTTTT 12240
 * V S C K Y R * S * R * L C S R * Y R F
 K C L A S I D E V S D D Y V Q D S T V L
 L S V L Q V * M K L A M I M F K I V P F

12241 GCAGGCTTTGCAAAGTGAGTTTGTAATATGGCTAGTTTTGTTGAATATGAAGTCGCAAA 12300
 A G F A K * V C K Y G * F C * I * S R K
 Q A L Q S E F V N M A S F V E Y E V A K
 C R L C K V S L * I W L V L L N M K S Q

12301 GAAAAATTTGGCTGATGCTAAAAATAGTGGTTCTGTTAATCAACAACAGATAAAACAGTT 12360
 E K F G * C * K * W F C * S T T D K T V
 K N L A D A K N S G S V N Q Q Q I K Q L
 R K I W L M L K I V V L L I N N R * N S

12361 AGAAAAAGCATGTAATATAGCTAAGTCTGTGTATGAACGTGATAAAGCTGTAGCTCGCAA 12420
 R K S M * Y S * V C V * T * * S C S S Q
 E K A C N I A K S V Y E R D K A V A R K
 * K K H V I * L S L C M N V I K L * L A

FIG. 2 CONT.

12421 ACTTGAACGTATGGCAGACCTAGCACTTACTAACATGTATAAAGAGGCTCGGATTAATGA 12480
T * T Y G R P S T Y * H V * R G S D * *
L E R M A D L A L T N M Y K E A R I N D
N L N V W Q T * H L L T C I K R L G L M

12481 TAAGAAGAGTAAAGTTGTTTCCGCTTTGCAGACAATGCTTTTTAGCATGGTTCGTAAATT 12540
* E E * S C F R F A D N A F * H G S * I
K K S K V V S A L Q T M L F S M V R K L
I R R V K L F P L C R Q C F L A W F V N

12541 GGATAATCAGGCTTTAAATTCTATTCTGGATAATGCTGTTAAAGGTGTGTACCTTIGAG 12600
G * S G F K F Y S G * C C * R L C T F E
D N Q A L N S I L D N A V K G C V P L S
W I I R L * I L F W I M L L K V V Y L *

12601 TGCTATTCAGCATTTGGCTGCTAATACTTTAACTATAGTAATACCAGATAAACAAGTTT 12660
C Y S S I G C * Y F N Y S N T R * T S F
A I P A L A A N T L T I V I P D K Q V F
V L F Q H W L L I L * L * * Y Q I N K F

12661 TGATAAAGTTGTTGATAATGTTTATGTTACATATGCTGGTAGTGTATGGCATATACAGAC 12720
* * S C * * C L C Y I C W * C M A Y T D
D K V V D N V Y V T Y A G S V W H I Q T
L I K L L I M F M L H M L V V Y G I Y R

12721 TGTTCAAGATGCTGATGGTATTAATAAACAGTTAACTGATATTAGTGTGATTCTAATTG 12780
C S R C * W Y * * T V N * Y * C * F * L
V Q D A D G I N K Q L T D I S V D S N W
L F K M L M V L I N S * L I L V L I L I

12781 GCCTCTGTTATCATTGCGAACAGGTATAATGAAGTTGCTAATGCTGTTATGCAGAATAA 12840
A S C Y H C E Q V * * S C * C C Y A E *
P L V I I A N R Y N E V A N A V M Q N N
G L L L S L R T G I M K L L M L L C R I

12841 TGAGTTGATGCCTCATAAATTAAAAATACAAGTTGTTAATAGTGGTTCTGATATGAATTG 12900
* V D A S * I K N T S C * * W F * Y E L
E L M P H K L K I Q V V N S G S D M N C
M S * C L I N * K Y K L L I V V L I * I

12901 TAATATTCCTACTCAATGTTATTATAATAATGGTAGTAGTGGTAGAATAGTTTATGCTGT 12960
* Y S Y S M L L * * W * * W * N S L C C
N I P T Q C Y Y N N G S S G R I V Y A V
V I F L L N V I I I M V V V V E * F M L

FIG. 2 CONT.

12961 TCTTAGTGATGTTGATGGTCTTAAGTATACTAAGATAATGAAAGATGATGGAAATTGTGT 13020
S * * C * W S * V Y * D N E R * W K L C
L S D V D G L K Y T K I M K D D G N C V
F L V M L M V L S I L R * * K M M E I V

13021 TGTTTTAGAGCTTGATCCTCCTTGTAATTTTCTATACAAGATGTTAAGGGACTTAAAT 13080
C F R A * S S L * I F Y T R C * G T * N
V L E L D P P C K F S I Q D V K G L K I
L F * S L I L L V N F L Y K M L R D L K

13081 TAAGTATCTTTATTTTATTAAAGGATGTAACACTTTAGCTAGAGGGTGGTTGTTGGTAC 13140
* V S L F Y * R M * H F S * R V G C W Y
K Y L Y F I K G C N T L A R G W V V G T
L S I F I L L K D V T L * L E G G L L V

13141 TTTATCTTCAACAATTAGATTGCAGGCTGGTGTGCTACTGAGTATGCAGCTAATCTTC 13200
F I F N N * I A G W C C Y * V C S * F F
L S S T I R L Q A G V A T E Y A A N S S
L Y L Q Q L D C R L V L L L S M Q L I L

13201 TATACTTTTATTATGTGCATTTTCTGTAGATCCTAAGAAAACCTATTATTAGATTATATACA 13260
Y T F I M C I F C R S * E N L F R L Y T
I L S L C A F S V D P K K T Y L D Y I Q
L Y F H Y V H F L * I L R K L I * I I Y

13261 ACAAGGTGGTGACCTATAATTAATTGTGTAAATGCTCTGTGATCATGCTGGTACTGG 13320
T R W C T Y N * L C * N A L * S C W Y W
Q G G V P I I N C V K M L C D H A G T G
N K V V Y L * L I V L K C S V I M L V L

13321 TATGGCCATTACTATTAAACCTGAGGCTACTATTAAACCAAGATTCTTATGGTGGTGCCTC 13380
Y G H Y Y * T * G Y Y * P R F L W W C L
M A I T I K P E A T I N Q D S Y G G A S
V W P L L L N L R L L L T K I L M V V P

13381 AGTTTGATTTATTGCCGTGCACGTGTAGAGCATCCAGATGTAGATGGTATATGTAAATT 13440
S L Y L L P C T C R A S R C R W Y M * I
V C I Y C R A R V E H P D V D G I C K L
Q F V F I A V H V * S I Q M * M V Y V N

13441 ACGTGGTAAATTTGTACAAGTCCCTTTGGGTATAAAAGATCCTATTCTTTATGTGTTAAC 13500
T W * I C T S P F G Y K R S Y S L C V N
R G K F V Q V P L G I K D P I L Y V L T
Y V V N L Y K S L W V * K I L F F M C *

FIG. 2 CONT.

13501 ACATGATGTTTGTCAAGTCTGTGGTTTTTGGAGAGATGGCAGTTGTTCTGTGTAGGTTT 13560
T * C L S S L W F L E R W Q L F L C R F
H D V C Q V C G F W R D G S C S C V G S
H M M F V K S V V F G E M A V V P V * V

13561 AAGTGTGCGTGTTC AATCTAAAGATT TAAATTTTAAACGGGTTTCGGGGTACTAGTGTG 13620
K C R C S I * R F K F F K R V R G T S V
S V A V Q S K D L N F L N G F G V L V *
Q V S L F N L K I * I F * T G S G Y * C

13621 AATGCCCGCTAGTACCTGTGCTAGTGGTTTATCTACTGATGTTCAATTAAGGGCATT 13680
N A R L V P C A S G L S T D V Q L R A F
M P G * Y P V L V V Y L L M F N * G H L
E C P A S T L C * W F I Y * C S I K G I

13681 GACATTTGTAATACCAATAGAGCTGGTATAGGTTTATATTATAAAGTGAATTGTTGCCGT 13740
D I C N T N R A G I G L Y Y K V N C C R
T F V I P I E L V * V Y I I K * I V A V
* H L * Y Q * S W Y R F I L * S E L L P

13741 TTTCAGCGTATAGATGACGACGGAATAAATTGGATAAGTTCTTTGTTGTCAAAGAAGT 13800
F Q R I D D D G N K L D K F F V V K R T
F S V * M T T V I N W I S S L L S K E L
F S A Y R * R R * * I G * V L C C Q K N

13801 AATTAGAAAGTTTATAATAAAGAGAAAACTTATTATGAGTTGACTAAAAGTTGTTGGTGT 13860
N L E V Y N K E K T Y Y E L T K S C G V
I * K F I I K R K L I M S * L K V V V L
* F R S L * * R E N L L * V D * K L W C

13861 GTGGCTGAACATGATTTCTTTACATTTGATATTGATGGTAGTCGCGTGCCACATATAGTT 13920
V A E H D F F T F D I D G S R V P H I V
W L N M I S L H L I L M V V A C H I * F
C G * T * F L Y I * Y * W * S R A T Y S

13921 CGTAGGAATCTTTCAAAGTATACTATGTTAGATCTTTGCTATGCATTGCGTCATTTTGAT 13980
R R N L S K Y T M L D L C Y A L R H F D
V G I F Q S I L C * I F A M H C V I L I
S * E S F K V Y Y V R S L L C I A S F *

13981 CGTAATGATTGTTCAATATTGTGTGAAATCTTTGTGAGTATGCTGATTGTAAAGAATCC 14040
R N D C S I L C E I L C E Y A D C K E S
V M I V Q Y C V K F F V S M L I V K N P
S * * L F N I V * N S L * V C * L * R I

FIG. 2 CONT.

14041 TACTTTTCTAAGAAAGATTGGTATGATTTTGTGAAAATCCTGATATTATTAATATATAT 14100
Y F S K K D W Y D F V E N P D I I N I Y
T F L R K I G M I L L K I L I L L I Y I
L L F * E R L V * F C * K S * Y Y * Y I

14101 AAAAAATTAGGCCCTATTTTAAATAGAGCTTTACTTAATACTGTCATTTTGCAGACACC 14160
K K L G P I F N R A L L N T V I F A D T
K N * A L F L I E L Y L I L S F L Q T P
* K I R P Y F * * S F T * Y C H F C R H

14161 TTAGTTGAAGTAGGTTTAGTTGGTGTTTTAACTTTAGATAACCAAGATTTGTATGGTCAA 14220
L V E V G L V G V L T L D N Q D L Y G Q
* L K * V * L V F * L * I T K I C M V N
L S * S R F S W C F N F R * P R F V W S

14221 TGGTATGATTTTGGTGATTTTATACAAACAGCCCCAGGGTTGGTGTGGCAGTTGCAGAT 14280
W Y D F G D F I Q T A P G F G V A V A D
G M I L V I L Y K Q P Q G L V W Q L Q I
M V * F W * F Y T N S P R V W C G S C R

14281 TCTTACTATTCTTATATGATGCCTATGTTGACTATGTGTCATGTATTAGATTGTGAATTA 14340
S Y Y S Y M M P M L T M C H V L D C E L
L T I L I * C L C * L C V M Y * I V N Y
F L L F L Y D A Y V D Y V S C I R L * I

14341 TTTGTTAATGATAGTTATAGACAATTCGATCTTGTACAGTATGATTTTACTGATTACAAG 14400
F V N D S Y R Q F D L V Q Y D F T D Y K
L L M I V I D N S I L Y S M I L L I T S
I C * * * L * T I R S C T V * F Y * L Q

14401 TTAGAGTTGTTTAATAAGTATTTTAAGTATTGGGGTATGAAGTATCATCCTAATACTGTG 14460
L E L F N K Y F K Y W G M K Y H P N T V
* S C L I S I L S I G V * S I I L I L W
V R V V * * V F * V L G Y E V S S * Y C

14461 GATTGTGATAATGATAGGTGATTATTTCATTGTGCTAATTTTAAATACTATTTAGTATG 14520
D C D N D R C I I H C A N F N I L F S M
I V I M I G V L F I V L I L I Y Y L V W
G L * * * * V Y Y S L C * F * Y T I * Y

14521 GTTTTACCTAATACTTGTTTTGGTCCCCTTGTAGACAAATTTTGTAGATGGGTGACCG 14580
V L P N T C F G P L V R Q I F V D G V P
F Y L I L V L V P L L D K F L * M V Y R
G F T * Y L F W S P C * T N F C R W C T

FIG. 2 CONT.

14581 TTTGTTGTTTCTATTGGTTACCATTACAAAGAGTTAGGTGTAGTTATGAACTTAGATGTT 14640
F V V S I G Y H Y K E L G V V M N L D V
L L F L L V T I T K S * V * L * T * M L
V C C F Y W L P L Q R V R C S Y E L R C

14641 GACACACACCGTTATCGTTTGTCTCTTAAAGATTACTTCTTTATGCAGCAGATCCTGCT 14700
D T H R Y R L S L K D L L L Y A A D P A
T H T V I V C L L K I Y F P M Q Q I L L
* H T P L S F V S * R F T S L C S R S C

14701 ATGCACGTTGCATCTGCTAGTGTCTGCTTGATTACGAACTTGTGTTTTAGTGTAGCT 14760
M H V A S A S A L L D L R T C C F S V A
C T L H L L V L C L I Y E L V V L V * L
Y A R C I C * C S A * F T N L L F * C S

14761 GCCATTACAAGTGGTATAAAAATTTCAAAGTGTAAAACAGGTAACTTTAACCAAGACTTT 14820
A I T S G I K F Q T V K P G N F N Q D F
P L Q V V * N F K L * N Q V T L T K T F
C H Y K W Y K I S N C K T R * L * P R L

14821 TACGAGTTTGTATAAAGTAAAGGCTTGTTTAAAGAGGGTAGTACAGTTGATTGAAACAT 14880
Y E F V K S K G L F K E G S T V D L K H
T S L L K V K A C L K R V V Q L I * N I
L R V C * K * R L V * R G * Y S * F E T

14881 TTTTCTTTTACTCAAGATGGTAATGCTGCAATTACTGATTATAATTATTATAAGTATAAT 14940
F F F T Q D G N A A I T D Y N Y Y K Y N
F S L L K M V M L Q L L I I I I I S I I
F F L Y S R W * C C N Y * L * L L * V *

14941 TTACCTACTATGGTTGATATTAAGCAGTTATTGTTTGTATTAGAAGTTGTTTATAAATAT 15000
L P T M V D I K Q L L F V L E V V Y K Y
Y L L W L I L S S Y C L Y * K L F I N I
F T Y Y G * Y * A V I V C I R S C L * I

15001 TTTGAAATTTATGATGGTGGTTGTATACCAGCATCACAAAGTTATTGTTAATAATTATGAT 15060
F E I Y D G G C I P A S Q V I V N N Y D
L K F M M V V V Y Q H H K L L L I I M I
F * N L * W W L Y T S I T S Y C * * L *

15061 AAAAGTCTGGTTATCCATTTAATAAATTTGGTAAAGCCAGACTTTATTATGAGGCATTA 15120
K S A G Y P F N K F G K A R L Y Y E A L
K V L V I H L I N L V K P D F I M R H Y
* K C W L S I * * I W * S Q T L L * G I

FIG. 2 CONT.

15121 TCATTTGAGGAACAGAATGAAATTTATGCATATACTAAACGTAATGTTCTGCCCCACCTTA 15180
S F E E Q N E I Y A Y T K R N V L P T L
H L R N R M K F M H I L N V M F C P P *
I I * G T E * N L C I Y * T * C S A H L

15181 ACTCAAATGAATTTAAATATGCTATCAGTGCTAAGAATAGAGCTCGCACTGTAGCAGGT 15240
T Q M N L K Y A I S A K N R A R T V A G
L K * I * N M L S V L R I E L A L * Q V
N S N E F K I C Y Q C * E * S S H C S R

15241 GTTTCATTCTTAGTACTATGACAGGCCGAATGTTCCATCAAAATGTTTGAAGAGTATA 15300
V S I L S T M T G R M F H Q K C L K S I
F L F L V L * Q A E C S I K N V * R V *
C F Y S * Y Y D R P N V P S K M F E E Y

15301 GCAGCTACCCGAGGTGTTCTGTTGTTATAGGAACCACTAAATTTATGGTGGTGGGAC 15360
A A T R G V P V V I G T T K F Y G G W D
Q L P E V F L L L * E P L N F M V V G T
S S Y P R C S C C Y R N H * I L W W L G

15361 GATATGTTACGTCATCTTATAAAGGATGTTGACAACCCTGTTCTTATGGGTGGGATTAT 15420
D M L R H L I K D V D N P V L M G W D Y
I C Y V I L * R M L T T L F L W V G I I
R Y V T S S Y K G C * Q P C S Y G L G L

15421 CCTAAATGTGATCGTGCTATGCCAAATATTTTGCGTATTGTTAGTAGTTAGTTTGGCC 15480
P K C D R A M P N I L R I V S S L V L A
L N V I V L C Q I F C V L L V V * F W P
S * M * S C Y A K Y F A Y C * * F S F G

15481 CGCAAACATGAATTTTGTGTTTACATGGTGATAGATTTTATCGCCTTGCGAATGAATGT 15540
R K H E F C C S H G D R F Y R L A N E C
A N M N F V V H M V I D F I A L R M N V
P Q T * I L L F T W * * I L S P C E * M

15541 GCTCAAGTTTGTGAGTGAAATAGTTATGTGTGGCGGTTGCTATTATGTTAAGCCTGGTGGT 15600
A Q V L S E I V M C G G C Y Y V K P G G
L K F * V K * L C V A V A I M L S L V V
C S S F E * N S Y V W R L L L C * A W W

15601 ACTAGCAGTGGTGATGCAACTACTGCTTTTGCTAATTCTGTTTTTAATATATGTCAGGCT 15660
T S S G D A T T A F A N S V F N I C Q A
L A V V M Q L L L L I L F L I Y V R L
Y * Q W * C N Y C F C * F C F * Y M S G

FIG. 2 CONT.

15661 GTTACTGCTAATGTTTGTCTCTTATGGCCTGTAATGGCCATAAGATTGAAGATTTAAGT 15720
V T A N V C S L M A C N G H K I E D L S
L L L M F V L L W P V M A I R L K I * V
C Y C * C L F S Y G L * W P * D * R F K

15721 ATACGCAATTTACAAAAACGCTTATACTCTAATGTTTATCGTACAGATTATGTTGATTAT 15780
I R N L Q K R L Y S N V Y R T D Y V D Y
Y A I Y K N A Y T L M F I V Q I M L I I
Y T Q F T K T L I L * C L S Y R L C * L

15781 ACATTTGTTAATGAGTATTATGAATTTTATGTAAGCATTTTAGTATGATGATTTTGAAGT 15840
T F V N E Y Y E F L C K H F S M M I L S
H L L M S I M N F Y V S I L V * * F * V
Y I C * * V L * I F M * A F * Y D D F E

15841 GATGATGGTGTGTCTGTATACTCTGATTATGCTAGTAAGGGTTATATAGCTAATATA 15900
D D G V V C Y N S D Y A S K G Y I A N I
M M V L S V I T L I M L V R V I * L I *
* * W C C L L * L * L C * * G L Y S * Y

15901 AGTGTTTTTCAACAAGTTTTGTACTATCAGAATAATGTCTTTATGTCTGAATCTAAATGT 15960
S V F Q Q V L Y Y Q N N V F M S E S K C
V F F N K F C T I R I M S L C L N L N V
K C F S T S F V L S E * C L Y V * I * M

15961 TGGGTTGAAAATGATATTACTAATGGTCCTCATGAATTTTGTTCCTCCCAACATACTATGTTA 16020
W V E N D I T N G P H E F C S Q H T M L
G L K M I L L M V L M N F V P N I L C *
L G * K * Y Y * W S S * I L F P T Y Y V

16021 GTTAAGATAGATGGTGATTATGTTTATTACCATATCCAGATCCTTCTAGAATTTTAGGA 16080
V K I D G D Y V Y L P Y P D P S R I L G
L R * M V I M F I Y H I Q I L L E F * E
S * D R W * L C L F T I S R S F * N F R

16081 GCTGGTGTGTTTGTGTGATGATTTATTGAAGACTGACAGTGTCTTTTGATAGAGCGCTTT 16140
A G C F V D D L L K T D S V L L I E R F
L V V L L M I Y * R L T V F F * * S A L
S W L F C * * F I E D * Q C S F D R A L

16141 GTAAGTCTAGCTATAGATGCTTACCCTTTAGTACATCATGAAAATGAAGAATACCAAAAA 16200
V S L A I D A Y P L V H H E N E E Y Q K
* V * L * M L T L * Y I M K M K N T K K
C K S S Y R C L P F S T S * K * R I P K

FIG. 2 CONT.

16201 GTCTTTCGTGTATATTTAGAATATATAAAAAAAGTGTATAATGATCTTGGTACTCAGATC 16260
V F R V Y L E Y I K K L Y N D L G T Q I
S F V Y I * N I * K N C I M I L V L R S
S L S C I F R I Y K K T V * * S W Y S D

16261 TTAGATAGTTATAGTGTTATTTAAGTACTTGTGATGGTTTAAAGTTTACTGAAGAATCA 16320
L D S Y S V I L S T C D G L K F T E E S
* I V I V L F * V L V M V * S L L K N H
L R * L * C Y F K Y L * W F K V Y * R I

16321 TTTTACAAGAATATGTATTTAAAAAGTGCCGTGATGCAGAGTGTAGGTGCATGCGTTGTT 16380
F Y K N M Y L K S A V M Q S V G A C V V
F T R I C I * K V P * C R V * V H A L F
I L Q E Y V F K K C R D A E C R C M R C

16381 TGTTTCATCACAACTTCTTTGCGTTGTGGCAGTTGTATACGTAAGCCTTTGTTATGTTGT 16440
C S S Q T S L R C G S C I R K P L L C C
V H H K L L C V V A V V Y V S L C Y V V
L F I T N F F A L W Q L Y T * A F V M L

16441 AAATGTTGTTATGACCATGTTATGGCAACTAATCATAAATATGTTTTGAGTGTCTCACCT 16500
K C C Y D H V M A T N H K Y V L S V S P
N V V M T M L W Q L I I N M F * V S H L
* M L L * P C Y G N * S * I C F E C L T

16501 TACGTTTGTAAATGCACCTAACTGTGATGTGAGTGTATGCACCAAATTATATTGGGCGGT 16560
Y V C N A P N C D V S D V T K L Y L G G
T F V M H L T V M * V M S P N Y I W A V
L R L * C T * L * C E * C H Q I I F G R

16561 ATGTCTTACTATTGTGAAAACCAATAAACCCATTATTCATTAAAGTTAGTTATGAATGGT 16620
M S Y Y C E N H K P H Y S F K L V M N G
C L T I V K T I N P I I H L S * L * M V
Y V L L L * K P * T P L F I * V S Y E W

16621 ATGGTCTTTGGTTTGTATAAACAATCTTGCACGGGTTACCTTATATAGATGATTTTAAT 16680
M V F G L Y K Q S C T G S P Y I D D F N
W S L V C I N N L A R V H L I * M I L I
Y G L W F V * T I L H G F T L Y R * F *

16681 AAGATAGCTAGTTGTAATGGACAGAAGTTGATGATTATGTTCTGGCAAATGAGTGTATT 16740
K I A S C K W T E V D D Y V L A N E C I
R * L V V N G Q K L M I M F W Q M S V L
* D S * L * M D R S * * L C S G K * V Y

FIG. 2 CONT.

16741 GAACGTTTAAAGTTATTTGCTGCAGAACTCAAAAGGCAACTGAAGAGGCTTTTAAACAA 16800
 E R L K L F A A E T Q K A T E E A F K Q
 N V * S Y L L Q K L K R Q L K R L L N K
 * T F K V I C C R N S K G N * R G F * T

16801 AGCTATGCTTCTGCTACCATTCAAGAGATTGTTAGTGATAGAGAAGTTATTTTGTGTTGG 16860
 S Y A S A T I Q E I V S D R E V I L C W
 A M L L L P F K R L L V I E K L F C V G
 K L C F C Y H S R D C * * * R S Y P V L

16861 GAGACAGGTAAAGTTAAACCACCACCTTAATAAAAATTATGTTTTACAGGCTACCATTTT 16920
 E T G K V K P P L N K N Y V F T G Y H F
 R Q V K L N H H L I K I M F S Q A T I L
 G D R * S * T T T * * K L C F H R L P F

16921 ACTAGTACTGGTAAGACAGTTTTAGGTGAGTATGTTTTGATAAAAGTGAATTAACAACTAAC 16980
 T S T G K T V L G E Y V F D K S E L T N
 L V L V R Q F * V S M F L I K V N * L T
 Y * Y W * D S F R * V C F * * K * I N *

16981 GGTGTGTATTACCGCGCTACAACCTTATAAACCTTTCTATAGGTGATGTTTTGTTTTTA 17040
 G V Y Y R A T T T Y K L S I G D V F V L
 V C I T A L Q L L I N F L * V M F L F *
 R C V L P R Y N Y L * T F Y R * C F C F

17041 ACATCACATTCTGTAGCTAGTTTAAAGTGACCTACACTTGTCCCACAAGAGAAGTATGCT 17100
 T S H S V A S L S A P T L V P Q E N Y A
 H H I L * L V * V H L H L S H K R T M L
 N I T F C S * F K C T Y T C P T R E L C

17101 AGTATAAGATTTTCTAGTGTTTATAGTGTTCATTGGTGTTCAAAATAATGTTGCTAAT 17160
 S I R F S S V Y S V P L V F Q N N V A N
 V * D F L V F I V F H W C F K I M L L I
 * Y K I F * C L * C S I G V S K * C C *

17161 TATCAGCACATTGGAATGAAACGTTATTGCACTGTTCAAGGTCCCCCTGGTACGGGAAAG 17220
 Y Q H I G M K R Y C T V Q G P P G T G K
 I S T L E * N V I A L F K V P L V R E S
 L S A H W N E T L L H C S R S P W Y G K

17221 TCTCATCTTGCTATAGGTCTAGCTGTTTATTACTACACAGCACGTGTAGTTTATACTGCT 17280
 S H L A I G L A V Y Y Y T A R V V Y T A
 L I L L * V * L F I T T Q H V * F I L L
 V S S C Y R S S C L L L H S T C S L Y C

FIG. 2 CONT.

17281 GCTAGTCATGCTGCTGTAGATGCATTGTGTGAAAAAGCTTATAAGTTTTTAAATATTAAC 17340
A S H A A V D A L C E K A Y K F L N I N
L V M L L * M H C V K K L I S F * I L T
C * S C C C R C I V * K S L * V F K Y *

17341 GATTGTACACGTATTATTCCTGCTAAAGTTCGTGTAGATTGTTATGATAAGTTTAAAT 17400
D C T R I I P A K V R V D C Y D K F K I
I V H V L F L L K F V * I V M I S L K L
R L Y T Y Y S C * S S C R L L * * V * N

17401 AATGATACCACTTGTAAGTATGTTTTTACCACAATAAATGCATTACCAGAGTTGGTTACA 17460
N D T T C K Y V F T T I N A L P E L V T
M I P L V S M F L P Q * M H Y Q S W L Q
* * Y H L * V C F Y H N K C I T R V G Y

17461 GATATTGTTGTTGTTGATGAAGTTAGTATGCTTACTAATTATGAATTGCTCTGTATATAAT 17520
D I V V V D E V S M L T N Y E L S V I N
I L L L L M K L V C L L I M N C L L * M
R Y C C C * * S * Y A Y * L * I V C Y K

17521 GCTCGTATTAAAGCTAAACATTATGTATATATTGGAGATCCTGCTCAATTACCTGCACCA 17580
A R I K A K H Y V Y I G D P A Q L P A P
L V L K L N I M Y I L E I L L N Y L H H
C S Y * S * T L C I Y W R S C S I T C T

17581 CGTGTGCTGTTGAGCAAGGGTTCTTTAGAACCTAGGCACTTCAATTCTATTACTAAAATA 17640
R V L L S K G S L E P R H F N S I T K I
V C C * A R V L * N L G T S I L L L K *
T C A V E Q G F F R T * A L Q F Y Y * N

17641 ATGTGTTGTTTAGGTCCTGATATCTTTTGGGAAATTGTTATAGGTGCTCTAAAGAAAT 17700
M C C L G P D I F L G N C Y R C P K E I
C V V * V L I S F W E I V I G V L K K L
N V L F R S * Y L F G K L L * V S * R N

17701 GTAGAACTGTTTCAGCATTGGTTTATGATAATAAACTCAAGGCTAAAAATGATAATAGT 17760
V E T V S A L V Y D N K L K A K N D N S
* K L F Q H W F M I I N S R L K M I I V
C R N C F S I G L * * * T Q G * K * * *

17761 TCATTATGTTTTTAAAGTATATTTTAAGGGACAGACAACACATGAGAGTTCAAGTGCTGTA 17820
S L C F K V Y F K G Q T T H E S S S A V
H Y V L K Y I L R D R Q H M R V Q V L *
F I M F * S I F * G T D N T * E F K C C

FIG. 2 CONT.

17821 AATATTCAACAGATATATCTAATTAGTAAATTTTAAAAGCTAATCCAGTTTGGGAATAGT 17880
 N I Q Q I Y L I S K F L K A N P V W N S
 I F N R Y I * L V N F * K L I Q F G I V
 K Y S T D I S N * * I F K S * S S L E *

17881 GCTGTTTTTATTAGTCCTTATAATAGTCAGAATTATGTTGCTAAGCGTGTGTTAGGTGTT 17940
 A V F I S P Y N S Q N Y V A K R V L G V
 L F L L V L I I V R I M L L S V F * V F
 C C F Y * S L * * S E L C C * A C F R C

17941 CAAACACAACTGTAGATTCTGCTCAAGGTTCCGAATATGATTATGTTATATATTCACAA 18000
 Q T Q T V D S A Q G S E Y D Y V I Y S Q
 K H K L * I L L K V R N M I M L Y I H K
 S N T N C R F C S R F G I * L C Y I F T

18001 ACAGCAGAAACAGCCCATTTCTGTTAATGTTAATCGATTTAATGTTGCCATAACTAGAGCC 18060
 T A E T A H S V N V N R F N V A I T R A
 Q Q K Q P I L L M L I D L M L P * L E P
 N S R N S P F C * C * S I * C C H N * S

18061 AAGAAGGGCAATTTTTGTGTTATGAGTAATATGCAATTATTTGAATCTCTTAATTTTATT 18120
 K K G I F C V M S N M Q L F E S L N F I
 R R A F F V L * V I C N Y L N L L I L L
 Q E G H F L C Y E * Y A I I * I S * F Y

18121 ACTCTACCTTTAGATAAAATTCAAAATCAAACCTTTACCTCGTTTGCATGACAACTAAT 18180
 T L P L D K I Q N Q T L P R L H C T T N
 L Y L * I K F K I K L Y L V C I A Q L I
 Y S T F R * N S K S N F T S F A L H N *

18181 CTTTTTAAAGATTGTAGTAAAAGTTGCTTAGGTTATCATCCAGCGCATGCCCCCTCATTT 18240
 L F K D C S K S C L G Y H P A H A P S F
 F L K I V V K V A * V I I Q R M P P H F
 S F * R L * * K L L R L S S S A C P L I

18241 TTAGCAGTTGATGATAAATATAAGGTTAATGAAAATTTGGCTGTAAATTTAAATATTGTT 18300
 L A V D D K Y K V N E N L A V N L N I C
 * Q L M I N I R L M K I W L * I * I F V
 F S S * * * I * G * * K F G C K F K Y L

18301 GAACCTGTTTTTAACATATTCTCGTTTAATATCTCTTATGGGTTTTAAATTAGATTGACT 18360
 E P V L T Y S R L I S L M G F K L D L T
 N L F * H I L V * Y L L W V L N * I * L
 * T C F N I F S F N I S Y G F * I R F D

FIG. 2 CONT.

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18361 CTTGATGGTTATTCTAAATTGTTTATTACTAAAGATGAAGCCATTAAACGTGTTAGAGGT 18420
      L D G Y S K L F I T K D E A I K R V R G
      L M V I L N C L L L K M K P L N V L E V
      S * W L F * I V Y Y * R * S H * T C * R

18421 TGGGTTGGTTTTGATGTTGAGGGCGCTCATGCTACTCGCGAAAACATTGGAACAACTTT 18480
      W V G F D V E G A H A T R E N I G T N F
      G L V L M L R A L M L L A K T L E Q T F
      L G W F * C * G R S C Y S R K H W N K L

18481 CCACITGCAAATAGGTTTTTCAACTGGTGTGGATTTTGTAGTTGAAGCTACTGGCTTATTT 18540
      P L Q I G F S T G V D F V V E A T G L F
      H C K * V F Q L V W I L * L K L L A Y L
      S T A N R F F N W C G F C S * S Y W L I

18541 GCTGAGAGAGATTGTTATACTTTTAAAAAACTGTAGCTAAAGCTCCTCCTGGTGAAAAA 18600
      A E R D C Y T F K K T V A K A P P G E K
      L R E I V I L L K K L * L K L L L V K N
      C * E R L L Y F * K N C S * S S S W * K

18601 TTTAAACATTTAATACCCCTTATGTCAAAAGGTCAAAAGTGGGATATTGTTAGAATTAGA 18660
      F K H L I P L M S K G Q K W D I V R I R
      L N I * Y P L C Q K V K S G I L L E L E
      I * T F N T P Y V K R S K V G Y C * N *

18661 ATTGTTCAAATGTTATCTGATTATCTTTTAGACCTTCTGATAGTGTAGTATTTATTACT 18720
      I V Q M L S D Y L L D L S D S V V F I T
      L F K C Y L I I F * T F L I V * Y L L L
      N C S N V I * L S F R P F * * C S I Y Y

18721 TGGTCTGCCAGTTTGAACCTTACTTGTTTAAAGGTATTTTGCTAAATTAGGCAGAGAGCTT 18780
      W S A S F E L T C L R Y F A K L G R E L
      G L P V L N L L V * G I L L N * A E S L
      L V C Q F * T Y L F K V F C * I R Q R A

18781 AATGTGAATGTGTGTTCTAATCGTGCTACATGCTACAATTCTAGAACTGGTTATTATGGT 18840
      N C N V C S N R A T C Y N S R T G Y Y G
      I V M C V L I V L H A T I L E L V I M V
      * L * C V F * S C Y M L Q F * N W L L W

18841 TGTGGCGCCATAGTTATACTTGTGATTATGTGTATAATCCACTTATTGTAGATATACAA 18900
      C W R H S Y T C D Y V Y N P L I V D I Q
      V G A I V I L V I M C I I H L L * I Y N
      L L A P * L Y L * L C V * S T Y C R Y T

```

FIG. 2 CONT.

18901 CAGTGGGGTTATACAGGTTCTTTAACTAGTAATCACGATATAATTTGTAATGTACATAAA 18960
Q W G Y T G S L T S N H D I I C N V H K
S G V I Q V L * L V I T I * F V M Y I K
T V G L Y R F F N * * S R Y N L * C T *

18961 GGTGCACATGTTGCGTCAGCTGATGCAATTATGACTCGTTGTTTAGCAATCTATGATTGT 19020
G A H V A S A D A I M T R C L A I Y D C
V H M L R Q L M Q L * L V V * Q S M I V
R C T C C V S * C N Y D S L F S N L * L

19021 TTTTGTAATCTGTTAATTGGAATTTAGAGTATCCAATAATTTCTAATGAGGTCAGTATA 19080
F C K S V N W N L E Y P I I S N E V S I
F V N L L I G I * S I Q * F L M R S V *
F L * I C * L E F R V S N N F * * G Q Y

19081 AATACATCTTGTAGGTTATTGCAGCGTGCATGCTTAAAGCTGCCATGCTATGTAATAGA 19140
N T S C R L L Q R V M L K A A M L C N R
I H L V G Y C S V S C L K L P C Y V I D
K Y I L * V I A A C H A * S C H A M * *

19141 TACAACCTTATGTTATGACATAGGCAATCCTAAAGGTTTAGCTTGTGTCAAAGATTATGAA 19200
Y N L C Y D I G N P K G L A C V K D Y E
T T Y V M T * A I L K V * L V S K I M N
I Q L M L * H R Q S * R F S L C Q R L *

19201 TTAAATTTTATGATGCTTTTCTGTAGCCAAGTCTGTTAAACAGTTATTTTATGTCTAT 19260
F K F Y D A F P V A K S V K Q L F Y V Y
L N F M M L F L * P S L L N S Y F M S M
I * I L * C F S C S Q V C * T V I L C L

19261 GATGTGCATAAAGATAATTTTAAAGATGGTTTATGTATGTTTGGAAATTGTAATGTTGAT 19320
D V H K D N F K D G L C M F W N C N V D
M C I K I I L K M V Y V C F G I V M L I
* C A * R * F * R W F M Y V L E L * C *

19321 AAATATCCATCTAATTCAATTGTTTGTAGATTGACACTCGAGTGTAAATAAATTAAAC 19380
K Y P S N S I V C R F D T R V L N K L N
N I H L I Q L F V D L T L E C * I N * T
* I S I * F N C L * I * H S S V K * I K

19381 CTTCCTGGATGTAATGGTGGTAGTTTGTATGTTAATAAACATGCATTCCTACTAATCCT 19440
L P G C N G G S L Y V N K H A F H T N P
F L D V M V V V C M L I N M H S I L I L
P S W M * W W * F V C * * T C I P Y * S

FIG. 2 CONT.

19441 TTTACTAGAACTGTTTTTGAAAATCTTAAGCCTATGCCTTTTTTCTATTATTCAGATACG 19500
 F T R T V F E N L K P M P F F Y Y S D T
 L L E L F L K I L S L C L F S I I Q I R
 F Y * N C F * K S * A Y A F F L L F R Y

19501 CCTTGTGTGTACGTAGATGGTTTAGAATCTAAACAAGTTGATTACGTTCCCTTTAAGAAGC 19560
 P C V Y V D G L E S K Q V D Y V P L R S
 L V C T * M V * N L N K L I T F L * E A
 A L C V R R W F R I * T S * L R S F K K

19561 GCCACTGTATCACACGGTGTAACTAGGTGGAGCTGTTTGTTCAAAGCATGCTGAAGAA 19620
 A T C I T R C N L G G A V C S K H A E E
 P L V S H G V I * V E L F V Q S M L K N
 R H L Y H T V * S R W S C L F K A C * R

19621 TATTGTAACACTCTTGAGTCTTATAATATAGTTACTACAGCAGGCTTTACTTTTTGGGTT 19680
 Y C N Y L E S Y N I V T T A G F T F W V
 I V T T L S L I I * L L Q Q A L L F G F
 I L * L P * V L * Y S Y Y S R L Y F L G

19681 TATAAGAATTTTGATTTTTATAATTTATGGAACACTTTTACTACGTTACAGAGTTTAGAA 19740
 Y K N F D F Y N L W N T F T T L Q S L E
 I R I L I F I I Y G T L L L R Y R V * K
 L * E F * F L * F M E H F Y Y V T E F R

19741 AACGTAATATATAACTTGGTTAATGTTGGTCATTATGATGGACGTACAGGTGAATTACCT 19800
 N V I Y N L V N V G H Y D G R T G E L P
 T * Y I T W L M L V I M M D V Q V N Y L
 K R N I * L G * C W S L * W T Y R * I T

19801 TGTGCTATTATGAATGACAAAGTTGTTGTTAAGATTAATAATGTAGATACTGTTATTTTT 19860
 C A I M N D K V V V K I N N V D T V I F
 V L L * M T K L L L R L I M * I L L F L
 L C Y Y E * Q S C C * D * * C R Y C Y F

19861 AAAAATAATACATCATTTCTACTAATATAGCTGTTGAATTGTTTACAAAACGTAGTATC 19920
 K N N T S F P T N I A V E L F T K R S I
 K I I H H F L L I * L L N C L Q N V V S
 * K * Y I I S Y * Y S C * I V Y K T * Y

19921 CGGCACCACCCTGAACTTAAGATTCTTAGAAAATTTGAACATTGATATTGTTGGAAGCAT 19980
 R H H P E L K I L R N L N I D I C W K H
 G T T L N L R F L E I * T L I F V G S M
 P A P P * T * D S * K F E H * Y L L E A

FIG. 2 CONT.

19981 GTCCTGTGGGATTATGTTAAAGATAGTTTGTGTTAGTCCACTTATGGTGTGTTGTAAA 20040
V L W D Y V K D S L F C S S T Y G V C K
S C G I M L K I V C F V V P L M V F V N
C P V G L C * R * F V L * F H L W C L *

20041 TACACAGATTTGAAGTTCATCGAAAATTTGAATATACTTTTGTGATGGTCGTGACACTGGC 20100
Y T D L K F I E N L N I L F D G R D T G
T Q I * S S S K I * I Y F L M V V T L A
I H R F E V H R K F E Y T F * W S * H W

20101 GCTTTAGAAGCTTTTAGAAAAGCAAGAAATGCTGTTTTATTAGTACTGAAAAATTAAGT 20160
A L E A F R K A R N G V F I S T E K L S
L * K L L E K Q E M V F L L V L K N * V
R F R S F * K S K K W C F Y * Y * K I K

20161 AGGTTATCAATGATTAAAGGTCCGCAACGAGCTGATTTAAATGGTGTGATTGTGGATAAA 20220
R L S M I K G P Q R A D L N G V I V D K
G Y Q * L K V R N E L I * M V * L W I K
* V I N D * R S A T S * F K W C D C G *

20221 GTTGGAGAACTCAAAGTTGAGTTTTGGTTGCTATGAGAAAAGATGGTGACGATGTTATC 20280
V G E L K V E F W F A M R K D G D D V I
L E N S K L S F G S L * E K M V T M L S
S W R T Q S * V L V R Y E K R W * R C Y

20281 TTCAGCCGAACAGACAGCCTATGCTCAAGCCATTACTGGAGCCCACAAGGTAATCTAGGT 20340
F S R T D S L C S S H Y W S P Q G N L G
S A E Q T A Y A Q A I T G A H K V I * V
L Q P N R Q P M L K P L L E P T R * S R

20341 GGTAATTGCGCGGTAATGTCATTGGTAATGATGCTCTAACACGTTTTACTATCTTTACT 20400
G N C A G N V I G N D A L T R F T I F T
V I A R V M S L V M M L * H V L L S L L
W * L R G * C H W * * C S N T F Y Y L Y

20401 CAGAGTCGTGTATTGTCAAGTTTTGAACCTCGCTCAGATTTAGAACGGGATTTATTGAT 20460
Q S R V L S S F E P R S D L E R D F I D
R V V Y C Q V L N L A Q I * N G I L L I
S E S C I V K F * T S L R F R T G F Y *

20461 ATGGATGATAATCTGTTTATTGCTAAATATGGTTTAGAAGACTATGCATTGATCATATA 20520
M D D N L F I A K Y G L E D Y A F D H I
W M I I C L L L N M V * K T M H L I I *
Y G * * S V Y C * I W F R R L C I * S Y

FIG. 2 CONT.

20521 GTTTATGGTAGTTTAAACCATAAAGTTATAGGAGGTTTGCATTGCTTATAGGCTTATTT 20580
V Y G S F N H K V I G G L H L L I G L F
F M V V L T I K L * E V C I C L * A Y F
S L W * F * P * S Y R R F A F A Y R L I

20581 CGTAGGAAAAAAAAATCTAATTTGTTAATTCAAGAGTTTTTACAGTATGATTCTAGTATT 20640
R R K K K S N L L I Q E F L Q Y D S S I
V G K K N L I C * F K S F Y S M I L V F
S * E K K I * F V N S R V F T V * F * Y

20641 CATTTCATATTTTATTACTGATCAGGAGTGTGGTAGTAGTAAGAGTGTGTTGTACAGTTATT 20700
H S Y F I T D Q E C G S S K S V C T V I
I H I L L L I R S V V V V R V F V Q L L
S F I F Y Y * S G V W * * * E C L Y S Y

20701 GATTTATTATTAGATGATTTTGTTCCTATTGTTAAGTCATTAAATTTGAGTTGTGTTAGT 20760
D L L L D D F V S I V K S L N L S C V S
I Y Y * M I L F L L L S H * I * V V L V
* F I I R * F C F Y C * V I K F E L C *

20761 AAAGTTGTTAATATTAATGTTGATTTTAAGGATTTTCAATTTATGTTGTGGTGAATGAT 20820
K V V N I N V D F K D F Q F M L W C N D
K L L I L M L I L R I F N L C C G V M I
* S C * Y * C * F * G F S I Y V V V * *

20821 AATAAAATTATGACTTTTTATCCTAAAATGCAAGCCACTAATGATTGGAAACCTGGCTAT 20880
N K I M T F Y P K M Q A T N D W K P G Y
I K L * L F I L K C K P L M I G N L A I
* * N Y D F L S * N A S H * * L E T W L

20881 TCTATGCCTGTTTTGTATAAGTATTTGAATGTTCCATTAGAGAGAGTCTCTTTATGGAAT 20940
S M P V L Y K Y L N V P L E R V S L W N
L C L F C I S I * M P H * R E S L Y G I
F Y A C F V * V F E C S I R E S L F M E

20941 TATGGTAAACCTATTAATTTGCCTACAGGCTGTATGATGAATGTTGCTAAGTACACTCAA 21000
Y G K P I N L P T G C M M N V A K Y T Q
M V N L L I C L Q A V * * M L L S T L N
L W * T Y * F A Y R L Y D E C C * V H S

21001 TTATGTCAGTATTTGAATACTACAACATTAGCTGTTCTGTTAATATGCGTGTGTTTACAT 21060
L C Q Y L N T T T L A V P V N M R V L H
Y V S I * I L Q H * L F L L I C V F Y I
I M S V F E Y Y N I S C S C * Y A C F T

FIG. 2 CONT.

21061 TTAGGTGCAGGGTCTGATAAAGAAGTAGCTCCAGGTTCTGCTGTTTTAAGACAGTGGTTA 21120
L G A G S D K E V A P G S A V L R Q W L
* V Q G L I K K * L Q V L L F * D S G Y
F R C R V * * R S S S R F C C F K T V V

21121 CCATCTGGTAGTATTCTTGTAGATAATGATTAAACCCATTGTTAGCGATAGTTTAGTT 21180
P S G S I L V D N D L N P F V S D S L V
H L V V F L * I M I * T H L L A I V * L
T I W * Y S C R * * F K P I C * R * F S

21181 ACTTATTTTGGAGATTGTATGACTTTACCATTGATGTGTCATTGGGATTGATAATATCT 21240
T Y F G D C M T L P F D C H W D L I I S
L I L E I V * L Y H L I V I G I * * Y L
Y L F W R L Y D F T I * L S L G F D N I

21241 GATATGTATGATCCTCTTACTAAAAATATTGCTGATTATAATGTGACTAAGGATGGGTTT 21300
D M Y D P L T K N I G D Y N V S K D G F
I C M I L L L K I L V I I M * V R M G F
* Y V * S S Y * K Y W * L * C E * G W V

21301 TTTACTTACATTGTGCTTTAATTCGTGATAAATTATCTTTGGGTGGTAGTGTAGCTATA 21360
F T Y I C H L I R D K L S L G G S V A I
L L T F V I * F V I N Y L W V V V * L *
F Y L H L S F N S * * I I F G W * C S Y

21361 AAAATTACAGAGTTTTCTTGGGAATGCTGATTATATAAATTAATGAGTTGTTTTGCATTT 21420
K I T E F S W N A D L Y K L M S C F A F
K L Q S F L G M L I Y I N * * V V L H F
K N Y R V F L E C * F I * I N E L F C I

21421 TGGACAGTTTTTTGTACTAATGTAAATGCTTCTTCTAGTGAAGGGTTTTTAATAGGTATA 21480
W T V F C T N V N A S S S E G F L I G I
G Q F F V L M * M L L L V K G F * * V *
L D S F L Y * C K C F F * * R V F N R Y

21481 AATTACCTGGGTAAATCTTCTTTGAAATAGATGGCAATGTTATGCATGCTAACTATTTG 21540
N Y L G K S S F E I D G N V M H A N Y L
I T W V N L L L K * M A M L C M L T I C
K L P G * I F F * N R W Q C Y A C * L F

21541 TTTTGGAGAAATAGTACAACATGGAATGGCGGTGCTTATAGTTTATTTGATATGACTAAA 21600
F W R N S T T W N G G A Y S L F D M T K
F G E I V Q H G M A V L I V Y L I * L N
V L E K * Y N M E W R C L * F I * Y D *

FIG. 2 CONT.

21601 TTTTCTTTGAAATTGGCTGGCACTGCTGTTGTTAATTTAAGACCAGATCAATTAAATGAT 21660
F S L K L A G T A V V N L R P D Q L N D
F L * N W L A L L L L I * D Q I N * M I
I F F E I G W H C C C * F K T R S I K *

21661 TTAGTTTATTCTCTTATTGAAAGAGGTAAATTATTAGTTCGCGATACGCGTAAAGAGATT 21720
L V Y S L I E R G K L L V R D T R K E I
* F I L L L K E V N Y * F A I R V K R F
F S L F S Y * K R * I I S S R Y A * R D

21721 TTTGTTGGTGATAGTCTTGTAATACTTGTAGATCTCATTAAATCTAAACTATGTTAAT 21780
F V G D S L V N T C * I S L N L N Y V N
L L V I V L * I L V R S H * I * T M L I
F C W * * S C K Y L L D L I K S K L C *

21781 TATTTTTTTTATTTTTTATTCTGTTATGGTTTTAATGAACCTCTTAATGTTGTGTCTCA 21840
Y F F I F L F L L W F * * T S * C C V S
I F L F F Y F C Y G F N E P L N V V S H
L F F Y F F I S V M V L M N L L M L C L

21841 TTTAAACCATGACIGGTTTTTATTGTTGATAGTCGTTCTGATTGTAACCATATTAATAA 21900
F K P * L V F I W * * S F * L * P Y * *
L N H D W F L F G D S R S D C N H I N N
I * T M T G F Y L V I V V L I V T I L I

21901 TTTAAAAATTAAAAATTTTGATTATTTGGATATTCACCCTAGTTTGTGCAACAATGGTAA 21960
F K N * K F * L F G Y S P * F V Q Q W *
L K I K N F D Y L D I H P S L C N N G K
I * K L K I L I I W I F T L V C A T M V

21961 GATTTTCATCTAGTGCCGGTGATTCTATTTTTTAAGAGTTTTCAITTCACCTCGATTTTATAA 22020
D F I * C R * F Y F * E F S F H S I L *
I S S S A G D S I F K S F H F T R F Y N
R F H L V P V I L F L R V F I S L D F I

22021 TTCACTGGCGAAGGTGATCAAATTATTTTTTATGAGGGTGTTAATTTTAATCCTTATCA 22080
L H W R R * S N Y F L * G C * F * S L S
Y T G E G D Q I I F Y E G V N F N P Y H
I T L A K V I K L F F M R V L I L I L I

22081 TAGATTTAAGTGTTCCTAATGGTAGTAAATGATGATGGCTTCTTAACAAGGTAAGATT 22140
* I * V F S * W * * * C M A S * Q G K I
R F K C F P N G S N D V W L L N K V R F
I D L S V F L M V V M M Y G F L T R * D

FIG. 2 CONT.

22141 TTATCGTGCCTTATATTCTAATATGGCCTTTTTTCGTTATCTTACTTTTGTGATATTCC 22200
 L S C L I F * Y G L F S L S Y F C * Y S
 Y R A L Y S N M A F F R Y L T F V D I P
 F I V P Y I L I W P F F V I L L L L I F

22201 TTATAATGTTTCTCTTTCTAAGTTTAATTCTTGTAAGTGATATTTTATCACTTAACAA 22260
 L * C F S F * V * F L * K * Y F I T * Q
 Y N V S L S K F N S C K S D I L S L N N
 L I M F L F L S L I L V K V I F Y H L T

22261 TCCTATTTTATTAATTATTCTAAGGAAGTTTATTTTACTTTATTAGGTTGTTCTCTTTA 22320
 S Y F Y * L F * G S L F Y F I R L F S L
 P I F I N Y S K E V Y F T L L G C S L Y
 I L F L L I I L R K F I L L Y * V V L F

22321 TTTAGTACCGCTTTGCCTTTTTAAATCTAACTTTAGTCAGTACTATTATAACATAGATAC 22380
 F S T A L P F * I * L * S V L L * H R Y
 L V P L C L F K S N F S Q Y Y Y N I D T
 I * Y R F A F L N L T L V S T I I T * I

22381 TGGCTCTGTTTATGGTTTTTCTAATGTTGTTTATCCTGATTAGACTGTATTTATATTTC 22440
 W L C L W F F * C C L S * F R L Y L Y F
 G S V Y G F S N V V Y P D L D C I Y I S
 L A L F M V F L M L F I L I * T V F I F

22441 TCTTAAACCAGGTTCTTATAAAGTTTCCACCACTGCACCTTTTTTATCCTTACCTACTAA 22500
 S * T R F L * S F H H C T F F I L T Y *
 L K P G S Y K V S T T A P F L S L P T K
 L L N Q V L I K F P P L H L F Y P Y L L

22501 AGCTCTCTGTTTGGATAAATCTAAACAATTTGTACCTGTACAGGTTGTTGATTCTAGATG 22560
 S S L F * * I * T I C T C T G C * F * M
 A L C F D K S K Q F V P V Q V V D S R W
 K L S V L I N L N N L Y L Y R L L I L D

22561 GAACAACGAGCGTGCCTCAGATATTTCTTTATCTGTTGCATGTCAATTGCCATATTGTTA 22620
 E Q R A C L R Y F F I C C M S I A I L L
 N N E R A S D I S L S V A C Q L P Y C Y
 G T T S V P Q I F L Y L L H V N C H I V

22621 TTTTCGCAATTCTTCTGCTAATTATGTTGGCAAGTATGATATTAACCACGGTGATAGTGG 22680
 F S Q F F C * L C W Q V * Y * P R * * W
 F R N S S A N Y V G K Y D I N H G D S G
 I F A I L L L I M L A S M I L T T V I V

FIG. 2 CONT.

22681 TTTTATTTCTATTTTATCTGGTCTTTTATATAATGTTTCTTGTTATTTTCATATTATGGTGT 22740
 F Y F Y F I W S F I * C F L Y F I L W C
 F I S I L S G L L Y N V S C I S Y Y G V
 V L F L F Y L V F Y I M F L V F H I M V

22741 ATTTTATATGATAATTTTACATCCATTGGCCCTATTATTCTTTTGGTAGGTGTCCTAC 22800
 I F I * * F Y I H L A L L F F W * V S Y
 F L Y D N F T S I W P Y Y S F G R C P T
 Y F Y M I I L H P F G P I I L L V G V L

22801 ATCTTCTATTATTAAACATCCAATTTGTGTTTATGATTTTTTGCCTATTATTTTACAAGG 22860
 I P Y Y * T S N L C L * F F A Y Y F T R
 S S I I K H P I C V Y D F L P I I L Q G
 H L L L L N I Q F V F M I F C L L F Y K

22861 TATTTTATTATGTTTAGCTTTACTTTTGTGTTTCTATTATTTTGTATATAACGA 22920
 Y F I M F S F T F C C F S I I F V I * R
 I L L C L A L L F V V F L L F L L Y N D
 V F Y Y V * L Y F L L F F Y Y F C Y I T

22921 TAAATCTCATTAAATCTAAACATGTTATTAATTATTTTATTTTGCCTACAACATTAGCT 22980
 * I S L N L N M L L I I F I L P T T L A
 K S H * I * T C Y * L F L F C L Q H * L
 I N L I K S K H V I N Y F Y F A Y N I S

22981 GTTATAGGTGATTTTAAATGTACTAATTTTGTCTATTAATGATTTAAACACCACAGTTTCCT 23040
 V I G D F N C T N F A I N D L N T T V P
 L * V I L I V L I L L L M I * T P Q F L
 C Y R * F * L Y * F C Y * * F K H H S S

23041 CGCATAAGTGAGTATGTTGTGGATGTTTCTTATGGTTTGGGTACATATTATATACTTGAT 23100
 R I S E Y V V D V S Y G L G T Y Y I L D
 A * V S M L W M F L M V W V H I I Y L I
 S H K * V C C G C F L W F G Y I L Y T *

23101 CGTGTTTATTTAAATACTACTATATTATTTACTGGTTATTCCCTAAATCTGGTGCCAAT 23160
 R V Y L N T T I L F T G Y F P K S G A N
 V F I * I L L Y Y L L V I S L N L V P I
 S C L F K Y Y Y I I Y W L F P * I W C Q

23161 TTTAGGGATCTATCTTTAAAGGTACTACATATTTGAGTACTCTTTGGTATCAGAAACCC 23220
 F R D L S L K G T T Y L S T L W Y Q K P
 L G I Y L * K V L H I * V L F G I R N P
 F * G S I F K R Y Y I F E Y S L V S E T

FIG. 2 CONT.

23221 TTTTATCTGATTTTAATAATGGTATTTTCTAGAGTTAAGAATACTAAGTTGTATGTT 23280
 F L S D F N N G I F S R V K N T K L Y V
 F Y L I L I M V F F L E L R I L S C M L
 L F I * F * * W Y F F * S * E Y * V V C

23281 AATAAACTTTGTATAGTGAGTTTAGTACTATAGTTATAGGTAGTGTTTTATTACAAC 23340
 N K T L Y S E F S T I V I G S V F I N N
 I K L C I V S L V L * L * V V F L L T T
 * * N F V * * V * Y Y S Y R * C F Y * Q

23341 TCTTATACTATTGTTGTTCAACCTCATAATGGTGTTTTGGAGATTACAGCTTGTCAATAC 23400
 S Y T I V V Q P H N G V L E I T A C Q Y
 L I L L L F N L I M V F W R L Q L V N T
 L L Y Y C C S T S * W C F G D Y S L S I

23401 ACTATGTGTGAGTATCCTCATACTATTTGTAATCTAAAGGTAGTTCTCGTAATGAATCT 23460
 T M C E Y P H T I C K S K G S S R N E S
 L C V S I L I L F V N L K V V L V M N L
 H Y V * V S S Y Y L * I * R * F S * * I

23461 TGGCATTTTGATAAATCTGAACCTTTGTGTCTGTTCAAGAAAAATTTACTTATAATGTT 23520
 W H F D K S E P L C L F K K N F T Y N V
 G I L I N L N L C V C S R K I L L I M F
 L A F * * I * T F V S V Q E K F Y L * C

23521 TCTACAGATTGGTTGTATTTTCATTTTATCAAGAACGTGGCACTTTTATGCTTATTAT 23580
 S T D W L Y F H F Y Q E R G T F Y A Y Y
 L Q I G C I F I F I K N V A L F M L I M
 F Y R L V V F S F L S R T W H F L C L L

23581 GCTGATTCTGGCATGCCTACTACTTTTTATTTAGTTTGTATCTTGGTACTCTTTTATCT 23640
 A D S G M P T T F L F S L Y L G T L L S
 L I L A C L L L F Y L V C I L V L F Y L
 C * F W H A Y Y F F I * F V S W Y S F I

23641 CATTATTATGTTTTGCCTTTGACTTGTAAATGCTATATCTTCTAATACTGATAATGAGACT 23700
 H Y Y V L P L T C N A I S S N T D N E T
 I I M F C L * L V M L Y L L I L I M R L
 S L L C F A F D L * C Y I F * Y * * * D

23701 TTACAATATTGGGTCACACCTTTGTCTAAACGCCAATATCTTCTTAAATTTGACAACCGT 23760
 L Q Y W V T P L S K R Q Y L L K F D N R
 Y N I G S H L C L N A N I F L N L T T V
 F T I L G H T F V * T P I S S * I * Q P

FIG. 2 CONT.

23761 GGTGTTATTACTAATGCTGTTGATTGTTCTAGTAGTTTCTTTAGCGAGATTCAATGTAAA 23820
G V I T N A V D C S S S F F S E I Q C K
V L L L M L L I V L V V S L A R F N V K
W C Y Y * C C * L F * * F L * R D S M *

23821 ACTAAATCTTTATTACCTAATACTGGTGTATTATGACTTATCTGGTTTTACTGTTAAGCCT 23880
T K S L L P N T G V Y D L S G F T V K P
L N L Y Y L I L V F M T Y L V L L L S L
N * I F I T * Y W C L * L I W F Y C * A

23881 GTTGCAACTGTACATCGTCGTATTCTGATTACCTGATTGTGACATTGATAAATGGCTT 23940
V A T V H R R I P D L P D C D I D K W L
L Q L Y I V V F L I Y L I V T L I N G L
C C N C T S S Y S * F T * L * H * * M A

23941 AACAAATTTAATGTACCCTCACCTCTTAATTGGGAACGTAAAATTTTTCTAATTGCAAC 24000
N N F N V P S P L N W E R K I F S N C N
T I L M Y P H L L I G N V K F F L I A T
* Q F * C T L T S * L G T * N F F * L Q

24001 TTFAATTGAGTACTTTGCTTCGTTTAGTTCACTGATTCTTTTCTGTGAATAATTTT 24060
F N L S T L L R L V H T D S F S C N N F
L I * V L C F V * F I L I L F L V I I L
L * F E Y F A S F S S Y * F F F L * * F

24061 GATGAATCTAAGATATATGGTAGTTGTTTTAAGACTATTGTTTTAGATAAATTGCCATA 24120
D E S K I Y G S C F K S I V L D K F A I
M N L R Y M V V V L R V L F * I N L P Y
* * I * D I W * L F * E Y C F R * I C H

24121 CCCAACTCCAGACGATCTGATTGTCAGTTGGGCAGTTCTGGTTTTCTGCAATCTTCTAAT 24180
P N S R R S D L Q L G S S G F L Q S S N
P T P D D L I C S W A V L V F C N L L I
T Q L Q T I * F A V G Q F W F S A I F *

24181 TATAAAATTGACACTACTTCTAGTTCTTGTCATTGTATTATAGTTTGCCCTGCAATTAAT 24240
Y K I D T T S S S C Q L Y Y S L P A I N
I K L T L L L V L V N C I I V C L Q L M
L * N * H Y F * F L S I V L * F A C N *

24241 GTTACTATTAATAATTATAATCCTTCTTCTGGAATAGAAGGTATGGTTTTAATAATTTT 24300
V T I N N Y N P S S W N R R Y G F N N F
L L L I I I I L L L G I E G M V L I I L
C Y Y * * L * S F F L E * K V W F * * F

FIG. 2 CONT.

24301 AATTTGAGCTCTCATAGTGTGTTTACTCACGTTATTGTTTTCTGTTAATAATACTTTT 24360
 N L S S H S V V Y S R Y C F S V N N T F
 I * A L I V L F T H V I V F L L I I L F
 * F E L S * C C L L T L L F F C * * Y F

24361 TGTCTTGTGCTAAACCTTCTTTTGCTTCAAGTTGCAAGAGTCATAAACCCACCTTCTGCT 24420
 C P C A K P S F A S S C K S H K P P S A
 V L V L N L L L L Q V A R V I N H L L L
 L S L C * T F F C F K L Q E S * T T F C

24421 TCCTGTCCTATTGGTACTAATTATCGTTCTTGTGAGAGTACTACTGTACTCGACCACACT 24480
 S C P I G T N Y R S C E S T T V L D H T
 P V L L V L I I V L V R V L L Y S T T L
 F L S Y W Y * L S F L * E Y Y C T R P H

24481 GACTGGTGTAGGTGTTCTTGTTTACCTGATCCTATAACTGCTTATGACCCTAGGTCTTGT 24540
 D W C R C S C L P D P I T A Y D P R S C
 T G V G V L V Y L I L * L L M T L G L V
 * L V * V F L F T * S Y N C L * P * V L

24541 TCTCAAAAAAAGTCTCTGGTGGTGTGGTGAACATTGTGCAGGGTTCGGTGTGTGATGAA 24600
 S Q K K S L V G V G E H C A G F G V D E
 L K K S L W L V L V N I V Q G S V L M K
 F S K K V S G W C W * T L C R V R C * *

24601 GAAAAGTGTGCTGTATTGGATGGATCATATAAGTTTCTTGTCTTTGTAGTACTGATGCC 24660
 E K C G V L D G S Y N V S C L C S T D A
 K S V V Y W M D H I M F L V F V V L M P
 R K V W C I G W I I * C F L S L * Y * C

24661 TTTCTAGGTGGTCTTATGACACTTGCCTCAGTAACAACCGTTGTAATATTTTTCTAAT 24720
 F L G W S Y D T C V S N N R C N I F S N
 F * V G L M T L A S V T T V V I F F L I
 L S R L V L * H L R Q * Q P L * Y F F *

24721 TTTATTTTAAATGGTATCAATAGTGGTACCCTTGTCTAATGATTTATTGCAGCCTAAT 24780
 F I L N G I N S G T T C S N D L L Q P N
 L F * M V S I V V P L V L M I Y C S L I
 F Y F K W Y Q * W Y H L F * * F I A A *

24781 ACTGAAGTTTTTACTGATGTTTGTGTGATTACGACCTTTATGGTATTACAGGACAAGGT 24840
 T E V F T D V C V D Y D L Y G I T G Q G
 L K F L L M F V L I T T F M V L Q D K V
 Y * S F Y * C L C * L R P L W Y Y R T R

FIG. 2 CONT.

24841 ATTTTAAAGAAGTTTCTGCTGTTTATTATAATAGTTGGCAAATCTTTGTATGATTCT 24900
I F K E V S A V Y Y N S W Q N L L Y D S
F L K K F L L F I I I V G K I F C M I L
Y F * R S F C C L L * * L A K S F V * F

24901 AATGGCAACATTATTGGTTTAAAGATTTTGTACTAATAAAACATATAATATTTCCCT 24960
N G N I I G F K D F V T N K T Y N I F P
M A T L L V L K I L L L I K H I I F S L
* W Q H Y W F * R F C Y * * N I * Y F P

24961 TGTATGCAGGAAGAGTTTCTGCTGCTTTTCATCAAATGCTTCCTCTTTGGCTTTACTT 25020
C Y A G R V S A A F H Q N A S S L A L L
V M Q E E F L L L F I K M L P L W L Y F
L L C R K S F C C F S S K C F L F G F T

25021 TATCGTAATTTAAATGTAGCTATGTTTTGAATAATATTTCTTTAACTACTCAGCCATAT 25080
Y R N L K C S Y V L N N I S L T T Q P Y
I V I * N V A M F * I I F L * L L S H I
L S * F K M * L C F E * Y F F N Y S A I

25081 TTTGATAGTTATCTTGGTTGCGTTTTTAATGCTGATAATTTAACTGATTATTCTGTTTCT 25140
F D S Y L G C V F N A D N L T D Y S V S
L I V I L V A F L M L I I * L I I L F L
F * * L S W L R F * C * * F N * L F C F

25141 TCTTGTGCTCTTCGATGGGTAGTGGTTTTTGTGTTGATTATAACTCACCTTCTTCTTCC 25200
S C A L R M G S G F C V D Y N S P S S S
L V L F A W V V V F V L I I T H L L L P
F L C S S H G * W F L C * L * L T F F F

25201 TCTTCGCGTCGTAAACGTAGAAGTATTTCTGCTTCTTATCGTTTTGTACTTTTGAACCC 25260
S S R R K R R S I S A S Y R F V T F E P
L R V V N V E V F L L L I V L L L L N P
L F A S * T * K Y F C F L S F C Y F * T

25261 TTTAATGTCAGTTTTGTAAATGACAGTATTGAGTCTGTGGTGGTCTTTATGAGATCAAA 25320
F N V S F V N D S I E S V G G L Y E I K
L M S V L L M T V L S L W V V F M R S K
L * C Q F C * * Q Y * V C G W S L * D Q

25321 ATTCCTCACTAATTTACTATAGTTGGTCAAGAGGAATTTATTCAAATAATTCCTCTAAA 25380
I P T N F T I V G Q E E F I Q T N S P K
F P L T L L * L V K R N L F K L I L L K
N S H * L Y Y S W S R G I Y S N * P S *

FIG. 2 CONT.

25381 GTTACTATTGATTGTTCTTTATTGTCTGTTCTAATTATGCAGCTTGCCATGACTTATTG 25440
V T I D C S L F V C S N Y A A C H D L L
L L L I V L Y L S V L I M Q L A M T Y C
S Y Y * L F F I C L F * L C S L P * L I

25441 TCAGAGTATGGCACTTTTGTGATAATATTAATAGTATTTTAGATGAAGTTAATGGTTTA 25500
S E Y G T F C D N I N S I L D E V N G L
Q S M A L F V I I L I V F * M K L M V Y
V R V W H F L * * Y * * Y F R * S * W F

25501 CTTGATACTACTCAATTGCATGTAGCTGATACTCTTATGCAAGGTGTCACACTTAGCTCC 25560
L D T T Q L H V A D T L M Q G V T L S S
L I L L N C M * L I L L C K V S H L A P
T * Y Y S I A C S * Y S Y A R C H T * L

25561 AATCTTAATACTAATTGCAATTTGATGTTGATAATATTAATTTTAAATCCCTAGTTGGA 25620
N L N T N L H F D V D N I N F K S L V G
I L I L I C I L M L I I L I L N P * L D
Q S * Y * F A F * C * * Y * F * I P S W

25621 TGTTTAGGTCCACACTGCGGTTCTTCTCTCGTTCTTTTTTTGAAGATTATTGTTTGAC 25680
C L G P H C G S S S R S F F E D L L F D
V * V H T A V L L L V L F L K I Y C L T
M F R S T L R F F F S F F F * R F I V *

25681 AAAGTTAACTTTTCAGATGTTGGTTTTGTTGAAGCTTATAACAATTGTACTGGTGGTAGT 25740
K V K L S D V G F V E A Y N N C T G G S
K L N F Q M L V L L K L I T I V L V V V
Q S * T F R C W F C * S L * Q L Y W W *

25741 GAAATTAGAGATCTTCTTTGTGTACAATCCTTTAATGGTATTAAAGTTTTGCCTCCTATT 25800
E I R D L L C V Q S F N G I K V L P P I
K L E I F F V Y N P L M V L K F C L L F
* N * R S S L C T I L * W Y * S F A S Y

25801 TTGTCTGAATCTCAAATTTCTGGTTACACCACAGCCGCTACTGTTGCTGCTATGTTTCCA 25860
L S E S Q I S G Y T T A A T V A A M F P
C L N L K F L V T P Q P L L L L L C F H
F V * I S N F W L H H S R Y C C C Y V S

25861 CCATGGTCAGCAGCTGGCATAACCATTTTCTCTTAATGTACAATATAGAATTAATGGT 25920
P W S A A A G I P F S L N V Q Y R I N G
H G Q Q Q L A Y H F L L M Y N I E L M V
T M V S S S W H T I F S * C T I * N * W

FIG. 2 CONT.

25921 TTGGGTGTTACTATGGATGTTCTTAATAAAATCAAAAGTTGATAGCTACTGCTTTTAAT 25980
L G V T M D V L N K N Q K L I A T A F N
W V L L W M F L I K I K S * * L L L L I
F G C Y Y G C S * * K S K V D S Y C F *

25981 AATGCTCTTCTTTCTATTGAGATGGTTTGTAGTCTACCAACTCTGCACTTGCTAAAATA 26040
N A L L S I Q N G F S A T N S A L A K I
M L F F L F R M V L V L P T L H L L K Y
* C S S F Y S E W F * C Y Q L C T C * N

26041 CAAAGTGTGTTAATTCTAATGCTCAAGCACTTAATAGTTTGTACAGCAATTATTTAAT 26100
Q S V V N S N A Q A L N S L L'Q Q L F N
K V L L I L M L K H L I V C Y S N Y L I
T K C C * F * C S S T * * F V T A I I *

26101 AAATTTGGTGCAATTAGTTCTTTTACAAGAAATTTTATCTCGTCTCGATGCTTTAGAG 26160
K F G A I S S S L Q E I L S R L D A L E
N L V Q L V L L Y K K F Y L V S M L * R
* I W C N * F F F T R N F I S S R C F R

26161 GCTCAGGTTGAGATTGATAGGCTTATTAATGGTCGTTTAACTGCTTTAAATGCTTIATGTC 26220
A Q V Q I D R L I N G R L T A L N A Y V
L R F R L I G L L M V V * L L * M L M S
G S G S D * * A Y * W S F N C F K C L C

26221 TCTCAACAGCTTAGTGATATTTCTCTGTAAAATTTGGTGCTGCTTTAGCTATGGAGAAG 26280
S Q Q L S D I S L V K F G A A L A M E K
L N S L V I F L L * N L V L L * L W R R
L S T A * * Y F S C K I W C C F S Y G E

26281 GTTAATGAGTGTGTTAAAAGTCAATCTCCTCGTATTAATTTTGTGGTAATGGTAATCAT 26340
V N E C V K S Q S P R I N F C G N G N H
L M S V L K V N L L V L I F V V M V I I
G * * V C * K S I S S Y * F L W * W * S

26341 ATTTTGTGTCATTAGTTCAAAATGCTCCTTATGGTTTGTGTTTATGCATTTTAGTTATAAA 26400
I L S L V Q N A P Y G L L F M H F S Y K
F C H * F K M L L M V C C L C I L V I N
Y F V I S S K C S L W F V V Y A F * L *

26401 CCTATTTCTTTTAAACTGTTTGTAGTAAGTCTGGTTTGTGTATATCAGGTGATGTAGGT 26460
P I S F K T V L V S P G L C I S G D V G
L F L L K L F * * V L V C V Y Q V M * V
T Y F F * N C F S K S W F V Y I R * C R

FIG. 2 CONT.

26461 ATTGCACCTAAACAAGGGTATTTTATTAAACATAATGATCATTGGATGTTCACTGGTAGT 26520
I A P K Q G Y F I K H N D H W M F T G S
L H L N K G I L L N I M I I G C S L V V
Y C T * T R V F Y * T * * S L D V H W *

26521 TCTTACTATTATCCTGAACCAATTCAGATAAAAATGTTGTTTTATGAATACTTGTCT 26580
S Y Y Y P E P I S D K N V V F M N T C S
L T I I L N Q F Q I K M L F L * I L V L
F L L L S * T N F R * K C C F Y E Y L F

26581 GTTAATTTTACTAAAGCGCCTCTTGTATTGGAATCATTCTGTACCAAAATGTCTGAT 26640
V N F T K A P L V Y L N H S V P K L S D
L I L L K R L L F I * I I L Y Q N C L I
C * F Y * S A S C L F E S F C T K I V *

26641 TTTGAATCTGAGTTATCTCATTGGTTTAAAAATCAAACATCCATTGCGCCTAATTTGACT 26700
F E S E L S H W F K N Q T S I A P N L T
L N L S Y L I G L K I K H P L R L I * L
F * I * V I S L V * K S N I H C A * F D

26701 TTAAATCTTCATACTATTAATGCTACTTTTTTAGATTGTATTATGAGATGAATCTTATT 26760
L N L H T I N A T F L D L Y Y E M N L I
* I F I L L M L L F * I C I M R * I L F
F K S S Y Y * C Y F F R F V L * D E S Y

26761 CAAGAGTCTATTAAGTCTTTGAATAATAGTTATATCAATCTTAAAGATATAGGTACATAT 26820
Q E S I K S L N N S Y I N L K D I G T Y
K S L L S L * I I V I S I L K I * V H M
S R V Y * V F E * * L Y Q S * R Y R Y I

26821 GAAATGTATGTAAATGGCCTTGGTATGTTTGGCTACTAATTTCTTTTCATTATAATA 26880
E M Y V K W P W Y V W L L I S F S F I I
K C M * N G L G M F G Y * F L F H L * Y
* N V C K M A L V C L A T N F F F I Y N

26881 TTCCTGTATTGCTCTTTTTTATATGTTGTTGTACTGGTTGTGGTTCIGCATGTTTTAGT 26940
F L V L L F F I C C C T G C G S A C F S
S L Y C S F L Y V V V L V V V L H V L V
I P C I A L F Y M L L Y W L W F C M F *

26941 AAATGTCATAATTGTTGTGATGAGTATGGTGGTCATCATGATTTTGTATCAAACATCT 27000
K C H N C C D E Y G G H H D F V I K T S
N V I I V V M S M V V I M I L L S K H L
* M S * L L * * V W W S S * F C Y Q N I

FIG. 2 CONT.

27001 CATGATGATTAGAAATCTCTTGTGAGATCTCATTAAATCTAAACTTTATTTATGGACGTTT 27060
H D D * N L L S D L I K S K L Y L W T F
M M I R I S C Q I S L N L N F I Y G R L
S * * L E S L V R S H * I * T L F M D V

27061 GGAGACCTAGCTACACACATTCTCTTGTATTAGAGAATTTGGTGTACAAACCTTGAAG 27120
G D L A T H I L L L L E N L V L Q T L K
E T * L H T F S C Y * R I W C Y K P * R
W R P S Y T H S L V I R E F G V T N L E

27121 ATTTGTGTCTAAAGTATAATTACTGTCAACCTATTGTTGGTTACTGTATTGTACCTTTAA 27180
I C V * S I I T V N L L L V T V L Y L *
F V S K V * L L S T Y C W L L Y C T F K
D L C L K Y N Y C Q P I V G Y C I V P L

27181 ATGTTTGGTGTGCGAAGTTGGCAAATTTGCTTCTCACTTTACATTACGTAGTCACGATA 27240
M F G V A S L A N L L L T L H Y V V T I
C L V S Q V W Q I C F S L Y I T * S R Y
N V W C R K F G K F A S H F T L R S H D

27241 TTTCCCATAGTAATAATTTTGGTGTGTGAAGTATTTACTACTTATGGTAATACTGTTT 27300
F P I V I I L V L * L V L L L M V I L F
F P * * * F W C C N * F Y Y L W * Y C F
I S H S N N F G V V T S F T T Y G N T V

27301 CTGAGGCTGTGTCTAGATTAGTTGAATCAGCTTCTGAATTTATTGTTTGGCGTGCAGAGG 27360
L R L C L D * L N Q L L N L L F G V Q R
* G C V * I S * I S F * I Y C L A C R G
S E A V S R L V E S A S E F I V W R A E

27361 CACTTAATAAGTATGGTTGATTATTTTCAATGATACTGCTTGGTACATAGGACAGATT 27420
H L I S M V D L F F N D T A W Y I G Q I
T * * V W L I Y F S M I L L G T * D R F
A L N K Y G * F I F Q * Y C L V H R T D

27421 TTAGTTTTAGTTTTATTTTGTCTTATTTCTTTAATCTTTGTTGTTGCTTTTTTAGCAACT 27480
L V L V L F C L I S L I F V V A F L A T
* F * F Y F V L F L * S L L L L F * Q L
F S F S F I L S Y F F N L C C C F F S N

27481 ATTAAGCTTTGTATGCAACTTTGTGGTTTTTGTAAATTTCTTTATTATTTCACCTTCGGCT 27540
I K L C M Q L C G F C N F F I I S P S A
L S F V C N F V V F V I S L L F H L R L
Y * A L Y A T L W F L * F L Y Y F T F G

FIG. 2 CONT.

27541 TACGTTTATAAAAGAGGTATGCAGTTGTATAAGTCTTATAGTGAACAAGTTATACCACCC 27600
Y V Y K R G M Q L Y K S Y S E Q V I P P
T F I K E V C S C I S L I V N K L Y H P
L R L * K R Y A V V * V L * * T S Y T T

27601 ACTTCAGATTATTTAATCTAAATCTAAACATTATGAATAAATCTTTTCTTCCTCAATTTA 27660
T S D Y L I * I * T L * I N L F F L N L
L Q I I * S K S K H Y E * I F S S S I Y
H F R L F N L N L N I M N K S F L P Q F

27661 CTTCTGATCAAGCTGTTACATTCTTAAAGAATGGAATTCTCTTTGGGTGTAATACTAC 27720
L L I K L L H S * K N G I S L W V * Y Y
F * S S C Y I L K R M E F L F G C N T T
T S D Q A V T F L K E W N F S L G V I L

27721 TTTTATTACTATCATATTGCAGTTCGGTTATACGAGCCGTAGTATGTTTGTATTATCTTA 27780
F L L L S Y C S S V I R A V V C L F I L
F Y Y Y H I A V R L Y E P * Y V C L S Y
L F I T I I L Q F G Y T S R S M F V Y L

27781 TCAAGATGATTATTCTTTGGCTTATGTGGCCATTGACTATCACCTTGACTATATTTAATT 27840
S R * L F F G L C G H * L S P * L Y L I
Q D D Y S L A Y V A I D Y H L D Y I * L
I K M I I L W L M W P L T I T L T I F N

27841 GTTTTATGCTTTGAATAATGCTTTTCTTGCAATTTCTATAGTGTTTACTATTATTCTA 27900
V F M L * I M L F L H F L * C L L L F L
F L C F E * C F S C I F Y S V Y Y Y F Y
C F Y A L N N A F L A F S I V F T I I S

27901 TTGTTATAIGGATTCTTTATTTTGTAAATAGTATTCGGCTTTTATTAGAACTGGCAGTT 27960
L L Y G F F I L L I V F G F L L E L A V
C Y M D S L F C * * Y S A F Y * N W Q L
I V I W I L Y F V N S I R L F I R T G S

27961 GGTGGAGTTTAAATCCAGAGACCAATAATCTTATGTGTATTGATATGAAAGGCAAGATGT 28020
G G V L I Q R P I I L C V L I * K A R C
V E F * S R D Q * S Y V Y * Y E R Q D V
W W S F N P E T N N L M C I D M K G K M

28021 TTGTTAGGCCAGTTATTGAGGACTATCACACATTAAGTCTACTGTTATTCGTGGTCATC 28080
L L G Q L L R T I T H * L L L L F V V I
C * A S Y * G L S H I N C Y C Y S W S S
F V R P V I E D Y H T L T A T V I R G H

FIG. 2 CONT.

28081 TTTATATACAGGGTGTCAAACCTGGCACTGGTTATACTCTTTTCAGATTGCCCCGTATATG 28140
 F I Y R V S N L A L V I L F Q I C P Y M
 L Y T G C Q T W H W L Y S F R F A R I C
 L Y I Q G V K L G T G Y T L S D L P V Y

28141 TTACTGTAGCTAAGGTGCAAGTACTTTGTACCTATAAACGTGCCTTTTTCAGATAAGTTAG 28200
 L L * L R C K Y F V P I N V P F * I S *
 Y C S * G A S T L Y L * T C L F R * V R
 V T V A K V Q V L C T Y K R A F L D K L

28201 ATGTTAATAGTGGTTTTCCTGTTTTTGTAAAGTCTAAAGTTGGTAACTATCGTTTACCGT 28260
 M L I V V L L F L L S L K L V T I V Y R
 C * * W F C C F C * V * S W * L S F T V
 D V N S G F A V F V K S K V G N Y R L P

28261 CTAGTAAACCTAGTGGTATGGATACTGCCTTGTTAAGAGCTTAAATCTAAACTATTAGGA 28320
 L V N L V V W I L P C * E L K S K L L G
 * * T * W Y G Y C L V K S L N L N Y * D
 S S K P S G M D T A L L R A * I * T I R

28321 TGTCTTATACTCCCGGTCATTATGCTGGAAGTAGAAGCTCCTCTGGAAATCGTTCAGGAA 28380
 C L I L P V I M L E V E A P L E I V Q E
 V L Y S R S L C W K * K L L W K S F R N
 M S Y T P G H Y A G S R S S S G N R S G

28381 TCCTCAAGAAAACCTTCTTGGGCTGACCAATCTGAGCGAAATTACCAAACCTTTAATAGAG 28440
 S S R K L L G L T N L S E I T K P L I E
 P Q E N F L G * P I * A K L P N L * * R
 I L K K T S W A D Q S E R N Y Q T F N R

28441 GCAGAAAAACCCAACCTAAATTCAGTGTGTCTACTCAACCACAAGGAAATCTATCCAC 28500
 A E K P N L N S L C L L N H K E I L S H
 Q K N P T * I H C V Y S T T R K Y Y P T
 G R K T Q P K F T V S T Q P Q G N T I P

28501 ATTATTCCTGTTCTCCGGGATCACTCAATTTCAAAAAGGTAGAGACTTTAAATTTTCAG 28560
 I I P G S P G S L N F K K V E T L N F Q
 L F L V L R D H S I S K R * R L * I F R
 H Y S W F S G I T Q F Q K G R D F K F S

28561 ATGGTCAAGGAGTTCCTTTCGGAGTACCCCTTCTGAAGCAAAAGGATATTGGT 28620
 M V K E F P L L S E Y P L L K Q K D I G
 W S R S S H C F R S T P F * S K R I L V
 D G Q G V P I A F G V P P S E A K G Y W

FIG. 2 CONT.

28621 ATAGACACAGCCGGCGTTCTTTTAAACAGCTGATGGTCAACAAAAGCAGTTGTTACCGA 28680
 I D T A G V L L K Q L M V N K S S C Y R
 * T Q P A F F * N S * W S T K A V V T E
 Y R H S R R S F K T A D G Q Q K Q L L P

28681 GATGGTATTTCTACTATCTCGGTACCGGCCATATGCCAATGCATCCTATGGTGAATCCC 28740
 D G I S T I S V P A H M P M H P M V N P
 M V F L L S R Y R P I C Q C I L W * I P
 R W Y F Y Y L G T G P Y A N A S Y G E S

28741 TCGAAGGGGTCTTCTGGGTTGCTAATCACCAAGCTGACACTTCTACTCCCTCCGATGTTT 28800
 S K G S S G L L I T K L T L L L P P M F
 R R G L L G C * S P S * H F Y S L R C F
 L E G V F W V A N H Q A D T S T P S D V

28801 CGTCAAGGGATCCTACTACTCAAGAAGCTATCCCTACTAGGTTTCCGCCTGGTACGATTT 28860
 R Q G I L L L K K L S L L G F R L V R F
 V K G S Y Y S R S Y P Y * V S A W Y D F
 S S R D P T T Q E A I P T R F P P G T I

28861 TGCCTCAAGGCTATTATGTTGAAGGCTCAGGAAGGTCTGCTTCTAATAGTCGACCAGGTT 28920
 C L K A I M L K A Q E G L L L I V D Q V
 A S R L L C * R L R K V C F * * S T R F
 L P Q G Y Y V E G S G R S A S N S R P G

28921 CACGTTCTCAATCACGTGGACCCAATAATCGTTCATTAAAGTAGAAGTAATTCTAATTTTA 28980
 H V L N H V D P I I V H * V E V I L I L
 T F S I T W T Q * S F I K * K * F * F *
 S R S Q S R G P N N R S L S R S N S N F

28981 GACATTCAAGATTCTATAGTAAACCTGATATGGCTGATGAGATCGCTAATCTTGTTTTAG 29040
 D I Q I L * * N L I W L M R S L I L P *
 T F R F Y S K T * Y G * * D R * S C F S
 R H S D S I V K P D M A D E I A N L V L

29041 CCAAGCTTGGTAAAGATTCTAAACCTCAGCAAGTCAAGCAAAATGCCAAGGAAATCA 29100
 P S L V K I L N L S K S L S K M P R K S
 Q A W * R F * T S A S H * A K C Q G N Q
 A K L G K D S K P Q Q V T K Q N A K E I

29101 GGCATAAAATTTTAAACAAACCTCGCCAAAAGCGAACTCCTAATAAACATTGTAATGTTC 29160
 G I K F * Q N L A K S E L L I N I V M F
 A * N F N K T S P K A N S * * T L * C S
 R H K I L T K P R Q K R T P N K H C N V

FIG. 2 CONT.

29161 AACAGTGTTTTGGTAAAAGAGGACCTTCTCAAAATTTTGGTAATGCTGAAATGTTAAAGC 29220
 N S V L V K E D L L K I L V M L K C * S
 T V F W * K R T F S K F W * C * N V K A
 Q Q C F G K R G P S Q N F G N A E M L K

29221 TTGGTACTAATGATCCTCAGTTTCCTATTCTTGCAGAATTAGCTCCTACACCAGGTGCTT 29280
 L V L M I L S F L F L Q N * L L H Q V L
 W Y * * S S V S Y S C R I S S Y T R C F
 L G T N D P Q F P I L A E L A P T P G A

29281 TTTTCTTTGGTTCTAAATTAGACTTGGTTAAAAGAGATTCCGAGGCTGACTCACCTGTTA 29340
 F S L V L N * T W L K E I P R L T H L L
 F L W F * I R L G * K R F R G * L T C *
 F F F G S K L D L V K R D S E A D S P V

29341 AAGATGTTTTTTGAACCTTCATTATTCTGGTTCTATTAGGTTTGATAGTACTTTACCAGGCT 29400
 K M F L N F I I L V L L G L I V L Y Q A
 R C F * T S L F W F Y * V * * Y F T R L
 K D V F E L H Y S G S I R F D S T L P G

29401 TTGAGACAATTATGAAAGTTCTTGAAGAGAATTAAATGCTTACGTTAATTCTAATCAGA 29460
 L R Q L * K F L K R I * M L T L I L I R
 * D N Y E S S * R E F K C L R * F * S E
 F E T I M K V L E E N L N A Y V N S N Q

29461 ACACTGATTCTGATTGCTTGAAGTTCTAAACCTCAGCGTAAAAGAGGTGTTAAACAATTAC 29520
 T L I L I R * V L N L S V K E V L N N Y
 H * F * F V E F * T S A * K R C * T I T
 N T D S D S L S S K P Q R K R G V K Q L

29521 CAGAACAGTTTGACTCTCTTAATTTAAGTGCTGGTACTCAGCACATTTCAAATGATTTTA 29580
 Q N S L T L L I * V L V L S T F Q M I L
 R T V * L S * F K C W Y S A H F K * F Y
 P E Q F D S L N L S A G T Q H I S N D F

29581 CTCCTGAGGATCATAGTTTACTTGCTACTCTTGATGATCCTTATGTAGAAGACTCTGTTG 29640
 L L R I I V Y L L L L M I L M * K T L L
 S * G S * F T C Y S * * S L C R R L C C
 T P E D H S L L A T L D D P Y V E D S V

29641 CTTAATGAGAATGAATCCTAATTCGACACTAGGTGGTAACCCCTCGCTATTATTTCGGAAT 29700
 L N E N E S * P D T R W * P L A I I R N
 L M R M N P N S T L G G N P S L L F G I
 A * * E * I L I R H * V V T P R Y Y S E

FIG. 2 CONT.

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29701 AGGACACTCTCTATCAGAATGAATTCCTTGCTGTAATAACAGATAGAGTAGGTTGTTACAG 29760
      R T L S I R M N S C C N N R * S R L L Q
      G H S L S E * I L A V I T D R V G C Y R
      * D T L Y Q N E F L L * * Q I E * V V T

29761 ACTATATATTAATTAGTAGAAATTTATATTTAGACATTTGATTGTTAGAGTAGTTATAA 29820
      T I Y * L V E I L Y L D I * L L E * L *
      L Y I N * * K F Y I * T F D C * S S Y K
      D Y I L I S R N F I F R H L I V R V V I

29821 GGTTTAGCTGTAGTATAAACGCCTCCGGGAAGAGCTATCAATTGTAGTGTTTAATATATA 29880
      G L A V V * T P P G R A I N C S V * Y I
      V * L * Y K R L R E E L S I V V F N I Y
      R F S C S I N A S G K S Y Q L * C L I Y

29881 TATTAGTATATGATTGAAATTAATTATAGCCTTTTGGAGGAATTACAAAAAAAAAAAAA 29940
      Y * Y M I E I N Y S L L E E L Q K K K K
      I S I * L K L I I A F W R N Y K K K K K
      I L V Y D * N * L * P F G G I T K K K K

29941 AA 29942

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K

FIG. 2 CONT.

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SEQ: 1   CTTATTCTCGCTTAACGCAGGCATGGCAGATAGTCGAATGCTAGAGAACAGTCTAGAGTA   60
          Y S R I A D T G D I L K R D R T L D *
          I L A F Q T R V T * * S V I E Q * I E
          F L L S N R G Y R R D A * S R K D S R M

61   ATTTAGATTGAAAAATTTGTTCTAAGGGACAATAGGTACGAACACTCACACCAAATTAG   120
          * I * V K * V L N G T I W A Q S H P K I
          N F R F K K F L I G Q * G H K H T H N L
          L D L S K L C S E R N D M S T L T T * D

121   TATTAGAACATAAAATGAAAGGTGTGAAAAGTAGAGAGACGGTCACTGCACAACCAACAG   180
          M I K Y K V K W V K * R E A L S T N T T
          * L R T N * K G C K E D R Q W H R T P Q
          Y D Q I K S E V S K M E R G T V H Q N D

181   GAGTCGCAGGGAGGGTATCCAGCGTTACTAATTTTGGTCGTTTATGCCAGAGCCGAAGTT   240
          R L T G G M P R L S * F W C I R D R S *
          G * R G E W L D C H N F G A F V T E A E
          E A D R G Y T A I I L V L L Y P R P K L

241   CACCCGCGGTCTTAAAGCAACCGACGAAGGCCTACGTCGCCTCCTCAACCGATCAGGATA   300
          T P A L I E N A A E P H L P P T P * D *
          L P R W F K T P Q K R I C R L L Q S T R
          H A G S N R Q S S G S A A S S N A L G I

301   CTTCACTCTACTCCCACCCAATACGGGGAGATGACCAGTTCGCTACCTTTCACAACCTAA   360
          S T L H P H T I G R * Q D L S P F H Q I
          H L * I L T P * A G R S T L R H F T N S
          F D S S P P N H G E V P * A I S L T P N

361   GCAAATACTATTAGTACACTTCTATCTAACAGCGACGTAAGAACCTGTTCTTACCGTACA   420
          R K H Y D H S S L N D S C E Q V L I A H
          E N I I I M H L Y I T A A N K S L F P M
          T * S L * T F I S Q R Q M R P C S H C T

421   CGTCAGTTTAGAATAGGCACTATAAAAAACAAGTACTTCTAGATGTACAACATCTTCAAGA   480
          A T L D * G H Y K Q E H L D V H Q L L E
          H L * I K D T I N K N M F I * M N Y F N
          C D F R I R S I K T * S S R C T T S T R

481   TTGATTTTGTGGCATTTCAGGCCATGCCGTTAAATTAATTTAGTGGAACGTATCGAA   540
          L * F L R L T R Y P L K L * I V K A Y S
          * S F C G Y L G T R C N * N F * R Q M A
          V L V A T F D P V A I K I L D G K C L K

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FIG. 3

541 CCCACCAAAAGGATTTC CATACAATACCCGAACAAGGCAAGTATGTTCTGATTGCAAT 600
P H N E * L T H * P S T G N M C S * V N
Q T T K R F P I N H A Q E T * V L S F T
P P K G L P Y T I P K N R E Y L V L R *

601 ACAACATGTAGTAGAAAGATACTGATGTAGATGATGATTAAACCCTTCTAAAAACCC 660
H Q V D D K * S * M * * * N Q H L N K P
I N Y M M K R H S C R S S I K T F I K Q
T T C * R E I V V D V V L K P S S K K P

661 AACCTAACATGGAAAACCAAAATACGGTAGAATACAAGTGTTTACCAAAGTTAAGACATC 720
N S Q V K Q N * A M K H E C I T E I R Y
T P N Y R K T K H W R I N V F P K L E T
Q I T G K P K I G D * T * L H N * N Q L

721 CAACATATAACTTCTCTCACTAAATTATTAAGTTTAAAAATTTAACTACTAATACTAAA 780
T T Y Q L S H N L L K L N * I Q H N H N
P Q I N F L T I * Y N * I K F K I I I I
N Y I S S L S K I I E F K L N S S * S K

781 ATCACATCTTCTACGAATACGACTCCAAGTACGACTCGGATTTCCATTTATAAGTGT TTT 840
* H L L H K H Q P E H Q A * L Y I N V F
K T Y F I S I S L N M S L R F T F I * L
L T S S A * A S T * A S G L P L Y E C F

841 TCGAATACGAAATGAATCTGTTATAGCACCATAATTTGGGCATGAAAAACATCTGGTCAT 900
L K H K V * V I D H Y * V R V K Q L G T
F S I S * K S L I T T N F G Y K K Y V L
A * A K S L C Y R P I L G T S K T S W Y

901 ACCAACACTGATAAGACCATTTAATCGTCTAACAGAAGTTTGAATACCAGTAATAAGAAA 960
H N H S N Q Y I L L N D E L K H D N N K
I T T V I R T F * C I T K L S I T M I R
P Q S * E P L N A S Q R * A * P * * E K

961 CGTTCATACTCTGTTTTTCGTCAGACATACCGAACGGTTAACACTGAAACTATAACATCA 1020
A L Y S V F A T Q I A Q W N H S Q Y Q L
Q L I H S L L L R Y P K G I T V K I N Y
C S I L C F C D T H S A L Q S K S I T T

1021 CCGAACCGTACATCAAGCACTAAGTGCTAAACAATACGCGGACGTCTGATATCGATGATA 1080
P K A H L E H N V I Q * A G A S * L * *
H S P M Y N T I * S K N H A Q L S Y S S
A Q C T T R S E R N T I R R C V I A V I

FIG. 3 CONT'D

1081 AACACCATAATTTATACAACGTGTTGGATGTCTTCTACATCATCTACCTCTACATCAATA 1140
K H Y * I H Q V V * L L H L L H L H L *
N T T N F I N C L R C F I Y Y I S I Y N
Q P I L Y T A C G V S S T T S P S T T I

1141 TGCACCTGGACATGTAAATAATAGACGACTACGTTATCAAAATTCGAAGGATCAAACTA 1200
V H V Q V N I I Q Q H L L K L A E * N S
Y T F R Y M * * R S I C Y N * L K R T Q
R S G T C K N D A S A I T K F S G L K I

1201 CTTTCAATACTGAGTATACCTACTAAAAAGATAATTTAGATATATATTACAACCTAAACAC 1260
S L * S E Y P H N K * * I * I Y H Q N T
H F N H S M H I I K R N F R Y I I N I Q
F T I V * I S S K E I L D I Y L T S K H

1261 ACTAACACCAAAAACAATACGTCATACCAATACATCTAACAAAATTACTATTAACACTAAA 1320
H N H N Q * A T H N H L N N * H Y N H N
T I T T K N H L I T I Y I T K I I I T I
S Q P K T I C Y P * T S Q K L S L Q S K

1321 AATACCAACCCAAAGTCCATTATACTACCTACCAAAAAGAACAGGTAACACAACATGTCA 1380
K H N P K L Y Y S P H N K K D M T N Y L
K I T P N * T I H H I T K R T W Q T T C
* P Q T E P L I I S P K E Q G N H Q V T

1381 AATACTGAGATCGCTTCAATTTCCGGGTTAGTAGACCACAATAAGGACTTTTAGGACACAA 1440
K H S * R L * L G I M Q H * E Q F D Q T
N I V R A F N F G L * R T N N R F I R H
* S E L S T L A W D D P T I G S F G T N

1441 TAAATGATTATCATGACTATGACAATTGGTACTAAGAAAATTAAACATACCAATAAGACA 1500
I * * Y Y Q Y Q * G H N K * N T H N N Q
* K S I T S I S N V M I R K I Q I T I R
N V L L V S V T L W S E K L K Y P * E T

1501 GTGTGGTAAACCAAGAACATATATAACCAGCGCGCAGGACCTAACACCTAAGGATATTA 1560
* V M Q N K Y I N T A A D Q I T S E * L
D C W K T R T Y I P R R T R S Q P N R Y
V G N P E Q I Y Q D G R G P N H I G I I

1561 ATTTAGAAGTCAGTTCAGAATACTACTAAACCAAATAAGTCCACATCATCCAACATTTAG 1620
* I K L * T K H H N P K N L H L L N Y I
N F R * D L R I I I Q N I * T Y Y T T F
L D E T L D * S S K T * E P T T P Q L D

FIG. 3 CONT'D

1621 ATAACAATTTCTTTGACGAGAATAATGAGTACGTGAAATGAATCTAATACAAGTTACATT 1680
 * Q * L F Q E * * E H V K S L N H E I Y
 R N N F F S S K N S M C K V * I I N L T
 I T L S V A R I V * A S * K S * T * H L

1681 CACACCATTAGAACTTGTCTTTACTATAAGAACCGCAATTATTAAGAACCACATCCGTTGA 1740
 T H Y D Q V F D Y E Q R * Y N K T Y A V
 L T T I K F L I M N K A N I I R P T P L
 H P L R S C F * I R P T L L E Q H L C S

1741 CAACGAATTATCTCCACTAATATTATACGAAGATTTTTTATAACTGAACAAACAATTCGC 1800
 T A * Y L H N Y Y A E L F Y Q S T Q * A
 Q Q K I S T I I I H K * F I N V Q K N L
 N S L L P S * L I S R F F I S K N T L R

1801 AGCAGCACTAAAACGAACGTTCAAACGTCAAACACCTCTACCAAAACATGGAAAAATGA 1860
 D H Q N Q K C T Q L K H L H N Q V K K V
 T T S I K S A L K C N T S I T K Y R K *
 R A S K A Q L N A T Q P S P K T G K K S

1861 TCTACCAAATTAAGGGGCATCAATAATAGATTAAGTCTCACCATAAAAGAAATGTAGAAA 1920
 L H N L E G Y N N D L E S H Y K R * M K
 * I T * N G T T I I * N L T T N E K C R
 S P K I G R L * * R I * L P I K K V D K

1921 CTACAGAGTTAAAAGTGTTCTTCAAAGACTATACACAAATTTTTACACATAAAACAAATA 1980
 S T E I K V L L K Q Y T N L F T Y K T *
 Q H R L K * L F N R I H T * F H T N Q K
 I D * N E C S T E S I H K F I H I K N I

1981 CCTGTCTCAAAGTCAACGATGTAAAATATATCTCGTAATACAATTATCCAACCAATGAGT 2040
 P C L K L Q * M K Y L A N H * Y T P * E
 H V S N * N S C K I Y L M I N I P Q N S
 S L T E T A V N * I S C * T L L N T V *

2041 TAAATTCAATAACCCATGATGTGAACAATTATTTACCAATTAACCAAATTATGGTACAA 2100
 I * T I P Y * V Q * Y F P * N T * Y W T
 L K L * Q T S C K N I F H N I P K I G H
 N L N N P V V S T L L I T L Q N L V M N

2101 TCTACGATCACGTGGACGATGTCCGACCGAAGAAATGGTTAATAACTTACCAGAAAAACA 2160
 L H * H V Q * L S A E K G I I S H D K Q
 * I S T C R S C A P K K V L * Q I T K K
 S A L A G A V P Q S R * W N N F P R K T

FIG. 3 CONT'D

2161 TCATAGAGTTGCGTTGAAATTAAAAACAACGAAATTATGGACTAATACGATTTTAAAATCA 2220
L I E L W S * N Q Q K L V Q N H * F K L
Y Y R L G V K I K N S * Y R I I S F N *
T D * A L K L K T A K I G S * A L I K T

2221 ATTATTTAAAAATGTGAAAAAATTCAATAATAATCTCACACAATGTCAACTACAAAATTT 2280
* Y I K C K K * T I I L T H * L Q H K L
N I F K V S K K L * * * L T N C N I N *
L L N * V K K L N N N S H T V T S T K F

2281 TCTATACGGACAAGAATTTTGATAATTACCAAATCAAACATAACATCCGTTATTCAAAT 2340
L Y A Q E * F * * H N L K Y Q L C Y T K
F I H R N K F S N I T * N T N Y A I L K
S I G T R L V I L P K T Q I T P L L N *

2341 ATTGCAATCATGTCCCAATTAAGGACCAAAACAAAATGGTACATTACGTGTCCTTGTGT 2400
Y R * Y L T L E Q N Q K V M Y H V P V V
I V N T C P * N R T K N * W T I C L F L
L T L V P N I G P K T K G H L A C S C C

2401 TTAAATAAAAAAACTTCCGCAACGTCTTAGACAATATCATCTTCTACTACAATAACTCTT 2460
F K N K Q L R Q L I Q * L L L H H * Q S
L N I K K F A N C F R N Y Y F I I N N L
I * K K S P T A S D T I T S S S T I S F

2461 ACAGTTTAGAAGAAATAGTAGAATACTCATAACAGTTGGTGGATTAGACATCTTTT 2520
H * I K K I M K H T N D V V * I Q L F F
I D F R R * * R I L I T L W R F R Y F F
T L D E K D D * S Y Q * G G L D T S F I

2521 AACATAATATCTATTATACATGTACCCATTACACCACTATTTAAAAAGGGATAACAGTA 2580
K Y * L Y Y T C P Y T H H Y I K G * Q *
N T N Y I I H V H T L T T I F K E R N D
Q I I S L I Y M P L H P S L N K G I T M

2581 CTTACTATTTTATAAACAGAAAATCTAGTCCGAACCGCAAAAGGTACACGTCCATCTTT 2640
S H Y F Y K D K L D P K A N E M H L Y F
H I I F I N T K * I L S P T K W T C T S
F S L F I Q R K S * A Q R K G H A P L F

2641 TCAATTAAAATGCTCTTTGGACAACAATACCTCTAAGGCAGAACTACTGTCAATTCCA 2700
L * N * R S V Q Q * P S E T K S S L * P
F N I K V L F R N N H L N R R Q H C N L
T L K L S F G T T I S I G D K I V T L T

FIG. 3 CONT'D

2701 ATACAACTAAATCTAAGATGAAACTACTATAAAATCCATTTCAAACAAGTCTTAAACT 2760
 * T Q N L N * K Q H Y K L Y L K N L I Q
 N H K I * I R S K I I N * T F N T * F K
 I N S K S E V K S S I K P L T Q E S N S

2761 TCATCTTTTCCCACAATGACATCTACTAAAACAACGACAACAAACACTACGATATCTCTT 2820
 L L F P H * Q L H N Q Q Q Q K H H * L S
 F Y F L T N S Y I I K N S N N T I S Y L
 T S F P T V T S S K T A T T Q S A I S F

2821 ACGAAATTTGAGAACATTTCTCGTAGGTCAACCAACCAATAGTTCAAGCACGTAAAAATTT 2880
 H K L S K Y L A D L P Q N D L E H M K L
 I S * V R T F L M W H N T I L N T C K *
 A K F E Q L S C G T T P * * T R A N K F

2881 ATTTGAATTACTCTTACAACAAATAAAATAAACTACTCCGACCACTACTTCGTTACCGGAG 2940
 Y V * H S H Q K N I Q H P Q H H L L P R
 I F K I L I N N I * K I L S T I F C H G
 L S L S F T T * K N S S A P S S A I A E

2941 AGCATACATAACATGAAAACGATAACTCCTACAACCTTCTGCAATAGTCATCACTTCGACA 3000
 E Y T N Y K Q * Q P H Q L R * * Y H L Q
 R T H I T S K S N L I N F V N D T T F S
 R I Y Q V K A I S S T S S T I L L S A T

3001 GCTTCTATGATAACTACCACAGCAACTTCTGTGATAATTACTGCTACTTCTACAACAATG 3060
 R L Y * Q H H R Q L C * * H R H L H Q *
 D F I S N I T D N F V S N I V I F I N N
 S S V I S P T T S S V I L S S S S T T V

3061 ACCACTGTTACTGCTACTTCTACAACAATGACCACTGTTACTGCTACTTCTACAACAATG 3120
 Q H C H R H L H Q * Q H C H R H L H Q *
 S T V I V I F I N N S T V I V I F I N N
 P S L S S S S T T V P S L S S S S T T V

3121 ACCACTGTTACTGCTACTTCTACAACAATGACCACTGTTACTGCTACTTCTACAACAATG 3180
 Q H C H R H L H Q * Q H C H R H L H Q *
 S T V I V I F I N N S T V I V I F I N N
 P S L S S S S T T V P S L S S S S T T V

3181 ACCACTGTTACTGCTACTTCTACAACAATGACCACTGTTACTGCTACTTCTACAACAATG 3240
 Q H C H R H L H Q * Q H C H R H L H Q *
 S T V I V I F I N N S T V I V I F I N N
 P S L S S S S T T V P S L S S S S T T V

FIG. 3 CONT'D

3241 ACCACTGTTACTGCTACTTCTACAACAATGACCACTGTTACTGCTACTTCTACAACAATG 3300
 Q H C H R H L H Q * Q H C H R H L H Q *
 S T V I V I F I N N S T V I V I F I N N
 P S L S S S S T T V P S L S S S S T T V

3301 ACCACTGTTACTGCTACTTCTACAACAATGACCACTGTTACTGCTACTTCTACAACAATG 3360
 Q H C H R H L H Q * Q H C H R H L H Q *
 S T V I V I F I N N S T V I V I F I N N
 P S L S S S S T T V P S L S S S S T T V

3361 ACCACTGTTACTGCTACTTCTACAACAATGACCACTGTTACTGCTACTTCTACAACAATG 3420
 Q H C H R H L H Q * Q H C H R H L H Q *
 S T V I V I F I N N S T V I V I F I N N
 P S L S S S S T T V P S L S S S S T T V

3421 ACCACTGTTACTGCTACTTCTACAACAATGACCACTGTTATTGCTACTTCTCTAACAATG 3480
 Q H C H R H L H Q * Q H C Y R H L S Q *
 S T V I V I F I N N S T V I V I F L N N
 P S L S S S S T T V P S L L S S S I T V

3481 ACCACTGTTACTACTGGTTTAAACAACAATGACCACTACTACATCTACTATAACTTTCATA 3540
 Q H C H H G F Q Q * Q H H H L H Y Q F Y
 S T V I I V L N N N S T I I Y I I N F T
 P S L S S W I T T V P S S T S S I S L I

3541 AATACTGAACTATGAATATTTTCGAGAAAATCAAAAATTACTACAGATATTACTACGAAA 3600
 K H S Q Y K Y L E K L K * H H R Y H H K
 N I V K I S I F S K * N K I I D I I I S
 * S K S V * L A R K T K L S T * L S A K

3601 CAAACAATCAATACCAAGATCACAACCTTTGTCTTTGTATATAAAATTTCAATTACCAAATAC 3660
 T Q * N H N * H Q F L F M N * L * H N I
 Q K N T I T R T N F C F C I K F N I T *
 N T L * P E L T S V S V Y K L T L P K H

3661 CAGTGGATGATAATGTGTATGATTAACAACCAACGCAAGACACAATGAACATTACGTCTT 3720
 T V * * * V Y * N N T A N Q T V Q L A S
 P * R S N C M S I T P Q T R H * K Y H L
 D G V I V C V L Q Q N R E T N S T I C F

3721 TAATGGAAAATTCAAATTCCTAAATCGATAACTTTTATACACCAATAGAATATTCCACCC 3780
 I V K * T * P N L * Q F Y T T I K Y P P
 F * R K L K L I * S N F I H P * R I L H
 N G K L N L S K A I S F I H N D * L T P

FIG. 3 CONT'D

3781 AATATTAGTTTCAAAACAACTAATAAATGACTGGTGATAAGGATTTCGATAACAAAACGG 3840
 N Y D F N Q Q N N V S W * E * L * Q K A
 T I I L T K N I I * Q G S N R F S N N Q
 * L * L K T S * K S V V I G L A I T K G

3841 AGTTCCACCAAAACATCGACTAAAACGAATAACCAAAAATTTGGTCAAACATAATTACG 3900
 E L H N Q L Q N Q K N T K L G T Q Y * H
 R L T T K Y S I K S I P K * V L K I N I
 * P P K T A S K A * Q N K F W N S I L A

3901 CATACGATTAACCACAACAAATTTTACACCAAAAAGAAAACATAATTTACCAACCTACG 3960
 T H * N T N N L I H N K K Q N L H N P H
 R I S I P T T * F T T K R K I * I T Q I
 Y A L Q H Q K F H P K E K S K F P K S A

3961 AAACAAAAAATACCTCTATAACACAGAGTACAAACATTCACACCTGTATTATACTGAGA 4020
 K T K K H L Y Q T E H K Y T H V Y Y S E
 S Q K K I S I N H R M N T L T S M I H S
 K N K * P S I T D * T Q L H P C L I V R

4021 TTATCGTCGCCTGAATGGAACATGTAATGTAAAAAGTAATAAACTACTGTAAAAACACG 4080
 L L L P S V K Y M V N K M I Q H C N K H
 * Y C R V * R T C * M K * * K I V I K T
 I A A S K G Q V N C K E N N S S L K Q A

4081 AAAAAACGTGGGGATTTTAAAAAATAACGACGTACACGACCTACATTTGCAAACAGT 4140
 K K C G * F F K * Q Q M H Q P H L R K D
 S K A G R F F N K N S C T S H I Y V N T
 K Q V G L F I K I A A H A T S T F T Q *

4141 AAGACATCGACAATATCCACTACTTGTATTATCTACCATTCAAACAATGATTTAAATCACC 4200
 N Q L Q * L H H V F L H Y T Q * * I * H
 M R Y S N Y T I F L Y I T L K N S F K T
 E T A T I P S S C I S P L N T V L N L P

4201 ACTATTTAACTAAATATCATCCAATACCTTACAGTAAATCATACAGAAGAAAACCTCAA 4260
 H Y I Q N * L L N H F T M * Y T K K Q T
 T I F K I K Y Y T I S H * K T H R R K L
 S L N S K I T P * P I D N L I D E K S N

4261 TGGAGTTAACATACCAAAACACATATTGTGGATTACATACAAAACAATTTCCACTATAATA 4320
 V E I T H N T Y L V * H I N Q * L H Y *
 * R L Q I T Q T Y C R I Y T K N F T I N
 G * N Y P K H I V G L T H K T L P S I I

FIG. 3 CONT'D

4321 TTTACAACGATCTGAACAATTTGACTACAATAACAATTAGGACGATTACCCGTATACGA 4380
 L H Q * V Q * L Q H * Q * D Q * H A Y A
 Y I N S S K N F S I N N N I R S I P M H
 F T A L S T L A S T I T L G A L P C I S

4381 GGTACCACCACCTCAACGTTTTTCGATATCGACATCGACGTCCATTTTTTAAAGATTTCCT 4440
 G H H H L Q L L * L Q L Q L Y F I K * L
 E M T T S N C F S Y S Y S C T F F K R F
 W P P P T A F A I A T A A P L F N E L S

4441 TTGACGACGATACCAATTTAGATTTCCACAAACGGTTCATCCTCTAACAATACAAAGATG 4500
 F Q Q * P * I * L H K G L L L N N H K *
 F S S S H N F R F T N A L Y S I T I N R
 V A A I T L D L P T Q W T P S Q * T E V

4501 GCCACCATTTAATACATTTTGTGAAGAATTATAACATCCGGGACTACGATCTGTTCTACC 4560
 R H Y I I Y F L E * Y Q L G Q H * V L H
 G T T F * T F C N K I N Y A R I S S L I
 P P L N H L V I R L I T P G S A L C S P

4561 TTCTGTTAGAATACAAAACAATCGTGCACGAATATTCGTAGAATTATTAATACTAACAAC 4620
 F V I K H K T L V H K Y A D * Y N H N N
 S S L R I N Q * C T S I L M K I I I I T
 L C D * T K N A R A * L C R L L * S Q Q

4621 AAACAGATGAGAGTATAGCCGACCATATAAATCACAAGGACGACTACACAGTAATTGAAT 4680
 N T * E * I P Q Y I * H E Q Q H T M L K
 T Q R S E Y R S T Y K T N R S I H * * S
 K D V R M D A P I N L T G A S T D N V *

4681 GGAAGATCCACAACAACACTATTTGTTCAATAGGAACAATCATTATTATTTCTTCTAAAACT 4740
 G E L H Q Q Y V L * G Q * Y Y Y L L N Q
 V K * T N N I F L N D K N T I I F F I K
 R R P T T S L C T I R T L L L L S S K S

4741 ATAATAAGTTTTTACAGTTTAATGAAGTCAACAACCATGATTTTCGTAACCGACAATCTAA 4800
 Y * E F I D F * K L Q Q Y * L M P Q * I
 I N N L F T L N S * N N T S F C Q S N S
 I I * F H * I V E T T P V L A N A T L N

4801 TTGACGATTACATCCGGCACAATAATTTAAACTCTGTCTACGTATGTTTGAAAAAACTC 4860
 L Q * H L G H * * I Q S L H M C V K K S
 * S S I Y A T N N F K L C I C V F K K Q
 V A L T P R T I L N S V S A Y L S K K L

FIG. 3 CONT'D

4861 ACCACTACTAACAAAACAAAGTTTAAAGAAGACAATATGTTCTTCAAATAACGAAGCAGT 4920
H H H N N Q K L N K Q * V L L K I A E D
T T I I T K N * I R R N Y L F N * Q K T
P S S Q K T E F E E T I C S T K N S R *

4921 ACTATATGTTAACTTATTACTGCAAGCACTAATAACAACAGATTCTACTGATCAGAAGG 4980
H Y V I S Y H R E H N N T T * S S * D E
M I Y L Q I I V N T I I Q Q R L H S T K
S I C N F L S T R S * K N D L I V L R G

4981 ATTTCTAACCGCAGAATAGTTATTTTAACTACAATAATTGCCACAATTTTGACAATTCAT 5040
* L N A D * * Y I Q H * * R H * F Q * T
R F I P T K D I F K I N N V T N F S N L
L S Q R R I L L N S T I L P T L V T L Y

5041 AAAACTCACAGGATTAAGATAAATATATACATCAGTCCCATTCTGAAACCAATACATAC 5100
N Q T D * N * K Y I Y D P Y L S Q N H I
I K L T R I R N I Y T T L T F V K T I Y
K S H G L E I * I H L * P L S K P * T H

5101 ACTACCAAGAAAAATATTTTCGTTGACAATTAGTTCAAACACAAAATAATCGATTCTTCTA 5160
H H N K K Y L L Q * D L K H K I L * S S
T I T R K I F C S N I L N T N * * S L L
S P E K * L A V T L * T Q T K N A L F I

5161 TCTACAAAACGAATGACATCTACCACAATTAAAATTTAGATAAAGAGAATGACATCCACT 5220
L H K A * Q L H H * N * I * K E * Q L H
Y I N Q K S Y I T N I K F R N R K S Y T
S T K S V T S P T L K L D I E R V T P S

5221 TCAAAAACCATTTTATGAACCATTACAAAAGACACTACCGTAACTACAATGATTCAATTT 5280
L K Q Y F V Q Y H K R H H C Q H * * T L
F N K T F Y K T I N E T I A N I N S L *
T K P L I S P L T K Q S P M S T V L N F

5281 CACATCACTAAAAATACGGCTATTTTAAAAATATAGTCATACTTTTAAACAGAAATCGACT 5340
T Y H N K H R Y F K I D T H F N T K L Q
L T T I K I G I F N * I L I F I Q R * S
H L S K * A S L I K Y * Y S F K D K A S

5341 ATAAAGACGACATGTTTCAAGTAAACCCAACTAGTCGTTGTTAACGAACGAATAATATT 5400
Y K Q Q V F N M Q T Q D A V I A Q K N Y
I N R S Y L T * K P K I L L L Q K S I I
I E A T C L E N P N S * C C N S A * * L

FIG. 3 CONT'D

5401 AAAAAATTGTCATACATTTACCAGACATCAACAATTGCCAGGTAAAAAAGAAAACCTTGT 5460
N K L L I Y I T Q L Q * R D M K K K Q V
I K * C Y T F P R Y N N V T W K K R K F
K K V T H L H D T T T L P G N K E K S C

5461 CAGAGTATTATTAAACAATACACTTACATCGAACAGAATACAACGTCGTATAATTAGAATT 5520
T E Y Y N N H S H L K D * T A A Y * D *
L R M I I T I H I Y S T K H Q L M N I K
D * L L Q * T F T A Q R I N C C I L R L

5521 TAAATTATTTACCGTCACCGTCCTTCGTACCATACTTAAAGCAGACCGTCTGGTGTATC 5580
I * Y I A T A P L M T H I E H Q C V V Y
F K I F P L P L F C P I F K T S A S W M
N L L H C H C S A H Y S N R A P L G C L

5581 CAATCAACGAGAACAATAATCGATTTCAGTAAATTTAAACTACTTGGTAGTCTACGATG 5640
T L Q E Q K L * L D N * I Q H V M L H *
P * N S K N * S F T M K F K I F W * I S
N T A R T K A L P * K L N S S G D S A V

5641 ACTAAAATAAGCACAACAAAACCTTTGTTCCGACTAAATAGTCCACGTTAAACACTTAATCT 5700
Q N * E H Q K S V L Q N I L H L K H I L
S I K N T N N Q F L S I * * T C N T F *
S K I R T T K F C A S K D P A I Q S N S

5701 TGAATAAACACTAACACCATAATTGTTCTTTTCAGCACAACCACAACACTACGACAATACGT 5760
V * K H N H Y * V L F D H Q H Q H Q * A
F K N T I T T N F L F T T N T N I S N H
S I Q S Q P I L C S L R T P T S A T I C

5761 AAAACCATGTAATCGTTTCTGACTAGAAAAATTACCAATATTCTAACCGACATTAACACG 5820
N Q Y M L L S Q D K * H N Y S Q S Y N H
M K T C * C L S I K K I T I L N A T I T
K P V N A F V S R K L P * L I P Q L Q A

5821 TCCATCTTAACAGGTAACATGATTTAACTTACATGGTAAAACTAAACAAGATTATGAGG 5880
L Y F Q G N Y * I S H V M K S K N * Y E
C T S N D M T S F Q I Y W K Q N T R I S
P L I T W Q V L N F T G N K I Q E L V G

5881 AGACTCATTCCTAAATGGACTACTACAACAACGTCGATTGTACAAATACCCACATCCACA 5940
E S Y P N V Q H H Q Q L * C T * P H L H
R Q T L I * R I I N N C S V H K H T Y T
R L L S K G S S T T A A L M N I P T P T

FIG. 3 CONT'D

5941 TCCGGTAATATGTGTAACTTTACACCAAGTGGAAATGGTTGTAATACTACGAACATCACA 6000
L G N Y V N S I H N V K G V N H H K Y H
Y A M I C M Q F T T * R V L M I I S T T
P W * V C K F H P E G * W C * S A Q L T

6001 ATTTTTTATATGTCCACAATCACCAACAAATTGACTGACGAACATAGAATTTTAAATTG 6060
* F I Y L H * H N N L Q S S T D * F N L
N F F I C T N T T T * S V A Q I K F I *
L F Y V P T L P Q K V S Q K Y R L F K V

6061 GGTCTGAAAATGTAGATACAACCTGATTAATAAAAAACCTACTACAACCTTTACCAACGAAT 6120
G S K * M * T S * N N K P H H Q F P Q K
G L S K C R H Q S I I K Q I I N F H N S
W V K V D I N V L * K K S S T S I T A *

6121 ATTGGGACTAGAAAGTGTATAATAACACTATTACCATTGATAATATGTTTGGATAATA 6180
Y G Q D K V I N N H Y H Y T N Y L V * *
I V R I K * L I I T I I T L I I C F R N
L G S R E C Y * Q S L P L Y * V F G I I

6181 TTTCCGAGTCAAATTTGGTAAACGATTTCAACTGCCACAAATATGATTGAAATTCAATCA 6240
L P E T * V M Q * L Q R H K Y * S * T L
Y L S L K F W K S F N V T N I S V K L *
F A * N L G N A L T S P T * V L K L N T

6241 ACCTGTACTATAAACACGAGTTAACTTACTATTCAATCCAAAATTACATCTAAACGGCAA 6300
Q V H Y K H E I S H Y T L N * H L N A T
N S M I N T S L Q I I L * T K I Y I Q R
P C S I Q A * N F S L N P K L T S K G N

6301 ACAACTCATGTTTCATTGTGTCAGACCGACATCGATGACCACTACAACAAAACCGTAGACT 6360
Q Q T C L L L R A Q L * Q H H Q K P M Q
K N L V F Y C D P R Y S S T I N N Q C R
T S Y L T V T Q G T A V P S T T K A D S

6361 ACTAAATATACACTTTGCAATAAAATTTCTACACTTTGAAAACCATTCGGACAATAAAC 6420
H N I H S V N N * L I H F K Q Y A Q * K
I I * I H F T I K F S T F S K T L R N N
S K Y T F R * K L P H S V K P L G T I Q

6421 CAAAACAGTACTACTTCGTAGTAACTTAAGAGAATGAATAAAATTATTGGATCAAAATT 6480
T K D H H L M M S N E * K N * Y V * N *
P K T M I F C * Q I R K S I K I F R T K
N Q * S S A D N F E R V * K L L G L K L

FIG. 3 CONT'D

6481 TAGACTTTTATCTATATCACAAAACAGACAACCTAAGACATAGACTCCTCAGTGTCCATT 6540
 I Q F Y I Y H K T Q Q N Q I Q P T V L Y
 F R F I S I T N Q R N I R Y R L L * L T
 D S F L Y L T K D T S E T D S S D C P L

6541 ACACCAATGAAGACAATACCTTAGCGTCTAATCATGATTTCTCCAATTCAATTTCCACAC 6600
 H P * K Q * P I A S * Y * L P * T L P H
 I H N S R N H F R L N T S F L N L * L T
 T T V E T I S D C I L V L S T L N F P T

6601 ATCTTTCTGACAATTTTATCTTCTACGATAATAACAATTACTACTTTTATCAAGATAATT 6660
 * F S Q * F L L H * * Q * H H F Y N * *
 N S L S N F Y F I S N N N I I F I T R N
 L F V T L I S S A I I T L S S F L E I L

6661 CCAACAATTTTCAAATAGAAATCAACTACAAACCCTATACATAAACTGTCCAACACTAAT 6720
 P Q * F N I K L Q H K P Y T N S L N H N
 L N N F T * R * N I N P I H I Q C T T I
 T T L L K D K T S T Q S I Y K V P Q S *

6721 ACAACAAACCCAACGATTACTTAACAGTGC GGATCAATTTAGTGGTTGTCAATCCCTTAT 6780
 H Q K P Q * H I T V G L * I V L L * P I
 I N N P N S I F Q * A * N F * W C N P F
 T T Q T A L S N D R R T L D G V T L S Y

6781 ATATGCTATACCATAATTTGGATAATGATATGGATATCTAAACAATACAAATTCTCTACT 6840
 Y V I H Y * V * * * V * L N T I N L L H
 I Y S I T N F R N S Y R Y I Q * T * S I
 I R Y P I L G I V I G I S K N H K L S S

6841 ATTAGTTTGAGAAAATCAAGGATTTTAAAAATTTCGTTCTCGATATCTTAAAAATACCAAA 6900
 Y D F E K L E * F K * L L L * L I K H N
 I I L S K * N R F N K F C S S Y F K I T
 L * V R K T G L I K L A L A I S N * P K

6901 AAACCTCACCAACAAATAAATACAAAAATCAAATAATGTAAATGTTTACTATTTTGCTA 6960
 K S T T T * K H K * N I V N * L H Y F W
 K Q L P Q K N I N K T * * M K C I I F G
 K F H N N I * T K L K N C K V F S L V M

6961 AAAAATATGATGTCTTTATCGAAGATTCAAATGAAAATTAAACAAAACAAACCGAGAATT 7020
 K K Y * L F L K * T * K * N T K N P E *
 N K I S C F Y S R L K S K I Q K T Q S K
 K * V V S I A E L N V K L K N Q K A R L

FIG. 3 CONT'D

7021 TTTACGAAAAGTCTGTAAATCTACCTCATATAAATATTTTCCAAAAGAACAACATCGGTG 7080
F H K E S M * I S Y I * L L N E Q Q L W
F I S K L C K S P T Y K Y F T K K N Y G
F A K * V N L H L I N I F P K ~ R T T A V

7081 ACACAAAACAAAACCAATTAATAAACATATATTTACAATAAAAATCACTGAAAATAGA 7140
Q T K T K T * N K T Y L H * K * H S K D
S H K Q K P K I K Q I Y I N N K T V K I
T N K N Q N L K K Y I F T I K L S K * R

7141 AGGATTATAATCACAAAAGGATAAAAACACCCTTCTTAACAATACACCTATTTCCGATG 7200
E * Y * H K E * K Q P F F Q * T S L P *
K R I N T N K R N K H S S N N H P Y L S
G L I L T K G I K T P L I T I H I F A V

7201 AAAACCAAACCAATGTAAACACTAAAAATAAGATTCAATCCACATCCAAAATGTTCAGT 7260
K Q N P * L K H N K N * T L H L N * L D
S K T Q N C N T I K I R L * T Y T K C T
K P K T V I Q S K * E L N P T P K V L *

7261 AAAACATTACCATCAAAATATACACTTAACACAGTAAGACCAAACTATACAACCTATG 7320
N K Y H Y N * I H I T D N Q N Q Y T P Y
M K T I T T K Y T F Q T M R T K I H Q I
K Q L P L K I H S N H * E P K S I N S V

7321 TATACGTCGATATCTAAAACAAGTCATACTTCATCTATCTGCACAAAATAAACTAATACA 7380
M H L * L N Q E T H L L Y V H K I Q N H
C I C S Y I K N L I F Y I S T N * K I I
Y A A I S K T * Y S T S L R T K N S * T

7381 ATCAAATCAGTTTAAATTAACAACTTGAGCAATAACCAATAAGTAATATGTGTCATACCAA 7440
* N L * I L Q Q V R * Q N N M I C L I T
N T * D F * N N F E N N T I * * V C Y P
L K T L N I T S S T I P * E N Y V T H N

7441 AATAGGTAATAAAAACAGAATAACCAATGTTAATAAATGATGTACCAACGGACTAAACAA 7500
K D M I K D * Q N V I I * * M T A Q N T
K I W * K T K N T * L * K S C P Q R I Q
* G N N Q R I P K C N N V V H N G S K N

7501 ATACAATCTTTGATACGTAACCAACTAATCTAAATAACATAACATCGATTATACAATGG 7560
* T L F * A N T S * I * Q I Q L * Y T V
K H * F S H M P Q N S K N Y K Y S I H *
I N S V I C Q N I L N I T N T A L I N G

FIG. 3 CONT'D

7561 ACGAAAACAGAACAACGCCAAAATATATCAACAATGACGATACATATTTTCATCAACCAAA 7620
Q K Q R T A T K Y L Q * Q * T Y L L Q N
R S K D Q Q P K I Y N N S S H I F Y N T
A K T K N R N * I T T V A I Y L T T P K

7621 ATAATCCGTATAACAGATACCAACATTATTTGACCAACAAATAAAACAATATTTGCTTT 7680
* * A Y Q R H N Y Y L Q N N I K N Y V F
K N P M N D I T T I F S T T * K T I F S
I L C I T * P Q L L A P Q K N Q * L R F

7681 AACATCACAAGCACAATTACATCATGATAACAACCACCACATTAAGCAATAATACTATA 7740
N Y H E H * T Y Y * Q Q H H L E N N H Y
I T T N T N L T T S N N T T Y N T I I I
Q L T R T L H L V I T P P T I R * * S I

7741 ATGACGATTACCACCATGACCAAAAACACAATTTGTAGTTACCTTAACAAAATTAACGGT 7800
* Q * H H Y Q N K H * V D I S N N * N G
N S S I T T S T K T N F M L P I T K I A
V A L P P V P K Q T L C * H F Q K L Q W

7801 AAGAAAATTTGGTCCATTGTGAAAATATTGACATCTTCGACGATATCTTGAAAGATTTCT 7860
N K * V L Y C K * L Q L L Q * L V K * L
M R K F W T V S K Y S Y F S S Y F K R F
E K L G P L V K I V T S A A I S S E L S

7861 CGAATTTGCTGGACATTTAGGTTGACTACGAAGTGTAATACATCAATGACTATAATTCGT 7920
A * V V Q L D L Q H K V N H L * Q Y * A
L K F S R Y I W S I S * M I Y N S I N L
S L R G T F G V S A E C * T T V S I L C

7921 TCAACCAACATACTACGCAACAAGATACTATCTCTACCTGTCGCACAAATGCTACTACA 7980
L Q N Y S A N T R H Y L H V A H K R H H
L N T T H H T Q E I I S I S L T N V I I
T P Q I I R K N * S L S P C R T * S S T

7981 ACTACGATCAAATAAACATCTATAATTATTAGACAATGTAAGATTTCAATTTCAACAAGG 8040
Q H * N I Q L Y * Y D T V N * L * L Q E
N I S T * K Y I N I I Q * M R F N F N N
S A L K N T S I L L R N C E L T L T T G

8041 ATTAAACATACATCAACATCATCTCTCACTACGACTATCTCGATTAAAAGACTTACGACA 8100
* N T H L Q L L S H H Q Y L * N E S H Q
R I Q I Y N Y Y L T I S I S S I K Q I S
L K Y T T T T S L S A S L A L K R F A T

FIG. 3 CONT'D

8101 ACACAAAATACGTGTTAGTAACATATCCGGATATAATGAACATCTGTTTTCAATTAATG 8160
 Q T K H V I M T Y A * I V Q L C F T L *
 N H K I C L * Q I P R Y * K Y V F L * N
 T N * A C D N Y L G I N S T S L F N I V

8161 ATGTCGAACATTACCATAGAGACATTGGGTCTGATACAACTACAAATACAACATATGAAA 8220
 * L K Y H Y R Q L G S * T Q H K H Q Y K
 S C S T I T D R Y G L S H K I N I N I S
 V A Q L P I E T V W V I N S T * T S V K

8221 ATACAGAGTAAACTACAACATCTTTCTCAAAATTATTAACAATTGTAACGAGTACG 8280
 * T E N Q H Q Y F S N * Y N Q * C Q E H
 K H R M K I N I S L T K I I K N V N S M
 I D * K S T S L F L K L L K T L M A * A

8281 AAGAGAATCTCTCCACACGTTAATCTTTCCAAAATCTATGAAAACACCCTACACATGC 8340
 K E * L P H A I L F P K L Y K Q P I H V
 S R K S L T H L * F L N * I S K H S T Y
 E R L S P T C N S F T K S V K T P H T R

8341 ATTTACAACAAGGTAACATAAGTCTACAACCTTTGTTCTAAATAATGATTTAGATACTATAG 8400
 Y I N N W Q N L H Q F L I * * * I * S I
 T F T T G N I * I N F C S K N S F R H Y
 L H Q E M S E S T S V L N I V L D I I D

8401 ACGTCATCGACGACCAAACCTTAAATGACTACTTTTAATATTGTTAAACCATGGATGTAT 8460
 Q L L Q Q N P I * Q H F N Y C N P V * M
 R C Y S S T Q F K S I F I I V I Q Y R C
 A T A A P K S N V S S F * L L K T G V Y

8461 AAATTTCTCACTATTATAACATCGACGACTAAATCCACAAGAATATGTCTTACCACGATT 8520
 N L S H Y Y Q L Q Q N L H E * V S H H *
 I * L T I I N Y S S I * T N K Y L I T S
 K F L S L I T A A S K P T R I C F P A L

8521 CGTACATGTCCCATTACAACGATTCCGTCGATTATAAAGAACATATACCAAATAACTACG 8580
 A H V P Y H Q * P L * Y K K Y I T * Q H
 L M Y L T I N S L C S I N R T Y P K N I
 C T C P L T A L A A L I E Q I H N I S A

8581 AAAATTAGTTGAATGACGACTAAATGTCGTATTTAATTTTTTCGTACACAATTTTGACC 8640
 K * D V * Q Q N V A Y I L F L M H * F Q
 S K I L K S S I * L M F * F F C T N F S
 K L * S V A S K C C L N F F A H T L V P

FIG. 3 CONT'D

8641 GAACTTCAATTTTAACTGAAAATTATTCGTTCTCCGTTACAGGGATAAGAATGTTGTGG 8700
 S S T L I S K * Y A L P L H G * E * L V
 A Q L * F Q S K I L L L C T D R N K C C
 K F N F N V K L L C S A L T G I R V V G

8701 GAAAAGTGAATTTCCCTCCACAACATAACTCATTAAACAATATATATAATAAAAAACAATC 8760
 R K V * L L H Q I S Y N T I Y I I K Q *
 G K * K F S T N Y Q T I Q * I Y * K K N
 K E S L P P T T N L L K N Y I N N K T L

8761 AAATTAGACAAAATATAATAACACCCGAAATAACGGATGTATATCACAAATATTCAGACT 8820
 N L R N * I I T P K I A * M Y H K Y T Q
 T * D T K Y * Q P S * Q R C I T N I L R
 K I Q K I N N H A K N G V Y L T * L D S

8821 ATAAGTAAACGGACGAATACGATCAAAATTTCAATAACTATTACCACAACAATCTCTATA 8880
 Y E N A Q K H * N * L * Q Y H H Q * L Y
 I N M Q R S I S T K F N N I I T N N S I
 I * K G A * A L K L T I S L P T T L S I

8881 AAGTCAATTACTAAATACAAAACGATTATTTAAAAAGGTAAACTAGTTACCATACTCAG 8940
 K L * H N I N Q * Y I K G I Q D I T H T
 N * N I I * T K S I F K E L K I L P I L
 E T L S K H K A L L N K W N S * H Y S D

8941 GTGAAAACCCAGACAAATGATAGTATTAAGATACCTAACGGGATAACATCACCGTCAATA 9000
 W K Q T Q K S D Y N * P N G * Q L P L *
 G S K P R N V I M I R H I A R N Y H C N
 V K P D T * * * L E I S Q G I T T A T I

9001 CCTACTTCTATAGCCAAAGATGATACAAATTACAAGGATGATTTCAAAACTCTGTACCGAA 9060
 P H L Y R N * * T * H E * * L K S V H S
 H I F I D T R S H K I N R S F N Q S M A
 S S S I P E V I N L T G V L T K L C P K

9061 AGTACAAAATGTAAAAAATTGAATACGTAAACGATCACTATCACAAAGTCACGATATGTGG 9120
 E H K V N K L K H M Q * H Y H E T S Y V
 K M N * M K * S I C K S T I T N L A I C
 * T K C K K V * A N A L S L T * H * V G

9121 TGTATAAGTCTAAAGAATATTACTAAAAATACGATCACCAACACAAAATAGTAGAAACAC 9180
 V Y E S K K Y H N K H * H N H K I M K T
 W M N L N R I I I K I S T T T N * * R Q
 C I * I E * L S K * A L P Q T K D D K H

FIG. 3 CONT'D

9181 ATGATACAAATTTTCTCCACTACCATGTGGTGTAGGAATAACAATAAGTCTACCACAATA 9240
Y * T * F L H H Y V V D K N N N L H H *
T S H K F S T I T C W M R I T I * I T N
V I N L L P S P V G C G * Q * E S P T I

9241 CTTCTTACGAAGAAACATATGTAGAAACCAAGGTGTATGTGCAATATCGGAACGATTAAG 9300
S S H K K T Y M K P E V Y V N Y G Q * N
H L I S R Q I C R Q N W M C T I A K S I
F F A E K Y V D K T G C V R * L R A L E

9301 ATTACCAAAATATTCTAAAGGACTACAATAATCACTTCCATAACATGCATAACATTCTTG 9360
* H N * L I E Q H * * H L Y Q V Y Q L F
R I T K Y S K R I N N T F T N Y T N Y S
L P K I L N G S T I L S P I T R I T L V

9361 CGCGAGATACTGAATAACATCTCACCCACGTACACTTATGCGGCTTCTCCCATATACAAA 9420
A S * S K N Y L P H M H I R R L P Y I N
R A R H S I T S H T C T F V G F L T Y T
R E I V * Q L T P A H S Y A S S P I H K

9421 ATTAATAATTATCAAGGACCCAAACTTATTACTAATAATATCTTCATACGGACCTTGAAA 9480
* N * Y N R P K S Y H N N Y F Y A Q F K
K I K I T G P N Q I I I I I S T H R S S
L K L L E Q T K F L S * * L L I G P V K

9481 AACACCATCTCTAGAAAACTAAACAAATAGTTAAAAATCATCAAATTAAGCAGGATA 9540
K H Y L D K Q N T K D I K * Y N L E D *
K T T S I K K I Q K I L K K T T * N T R
Q P L S R K S K N * * N K L L K I R G I

9541 TCTAAAGAAAAGAGAATGACGATCAAGATAAAACCTCGATATAACCGATATCAACAACA 9600
L N R K E * Q * N * K Q L * I P * L Q Q
Y I E K R K S S T R N K S S Y Q S Y N N
S K K E R V A L E I K P A I N A I T T T

9601 GAACCAAAAAATAATAAATTATTTGAATTGCGACGAAAACCTCTAATATGATCACAACA 9660
R P K K N N L L V * A H K Q L N Y * H Q
D Q N K I I * Y F K L T S K S I I S T N
K T K * * K I F S L R A K P S * V L T T

9661 TCAATATTTACAACAACAAACCACATAATTAAGAATACGAAAAACAAAAGTTCAAAT 9720
L * L H Q Q K T Y * N E * A K Q K E L K
Y N Y I N N N P T N I K K H K K N K L N
T I F T T T Q H I L K R I S K T K * T *

FIG. 3 CONT'D

9721 AGGATAAACACGTACACAAATACGAACAAAAATAAAATACATTGTAACATAAAAGGAAG 9780
D * K H M H K H K N K N K H L M T N E K
I R N T C T N I S T K I K I Y C Q I K R
G I Q A H T * A Q K * K * T V N Y K G E

9781 ACTTTAATCACATTAATACGTAAACGTTACCTAACATAACACCACGATATTACGGAAA 9840
Q F * H L * A N A I S Q * T H H * L A K
R F N T Y N H M Q L P N N H I T S Y H R
S I L T I I C K C H I T I Y P A I I G K

9841 AACC AAAACACAGTGTATACATCGATACCAATAACGTTTGGTACAAAATACCAATAAAAG 9900
K T K H * M H L * P * Q L G H K I T I K
K P K T D C I Y S H N N C V M N * P * K
Q N Q T V Y T A I T I A F W T K H N N E

9901 TATAACATCCTTTTAACCACAATTACATACATCACTATCATGTAAACTTCTTTGTAGAGA 9960
M N Y S F Q H * H I Y H Y Y M Q L F M E
* I T P F N T N I Y T T I T C K F F C R
Y Q L F I P T L T H L S L V N S S V D R

9961 ATGATGAAAATACTAATGATTCTAAGAATAACATCTAATTCTTTAAGACAAAGACTACA 10020
* * K * S * * L N K N Y I L S N Q K Q H
K S S K H N S F I R I T S * L I R N R I
V V K I I V L S E * Q L N F F E T E S T

10021 ACGGATGTTATCTATAAACTCAAACATATTATTTCATAGCAATGATATCACCATTTTACCT 10080
Q R C Y I N S N T Y Y T D N S Y H Y F P
N G V I S I Q T Q I I L I T V I T T F H
A * L L Y K L K Y L L Y R * * L P L I S

10081 ATGACGACGGATATCTCTTCGCCGCACAAGAGTCAATCGATTTTCGATACCTTTGTAAATT 10140
Y Q Q R Y L L P T N E T L * L * P F M *
I S S G I S F R R T R L * S F S H F C K
V A A * L S A A H E * N A L A I S V N L

10141 AGTGTTATTACCATTACTACAGAATATGGTTGGAGGATGTCGTAGACAAAGATGTAGAAA 10200
D C Y H Y H H R I G V E * L M Q K * M K
I V I I T I I D * V L R R C C R N R C R
* L L P L S T K Y W G G V A D T E V D K

10201 AAACGTTAGTCCATAACATTTCTACCATAGAGGATGCAGTTTTTAACTTGGAACATAACA 10260
K A I L Y Q L S P I E * T L F Q V K Y Q
K Q L * T N Y L H Y R R R * F N F R T N
K C D P I T F I T D G V D F I S G Q I T

FIG. 3 CONT'D

10261 ATCACAATGAATACCATCATACTGAAACTTACCAAATACCAATCTACTGTTTCAAATAAC 10320
 * H * K H Y Y S K S H N I T L H C L K N
 N T N S I T T H S Q I T * P * I V F N I
 L T V * P L I V K F P K H N S S L T * Q

10321 AGGAGCAGTACAATATACAAGTAGGAGATTATACTTGCTTGACTAATAAGACGGAATAA 10380
 D E D H * I N M R * Y S R V Q N N Q R I
 T R T M N Y T * G R I H V F R I I R G *
 G R * T I H E D E L I F S G S * E A K N

10381 CACATCTCAATGAGATCCACTAAAATGATATTACAGACCAGCCTACTCAAATTGTCAACA 10440
 T Y L * E L H N * * L T Q D S S N L L Q
 Q T S N S * T I K S Y H R T P H T * C N
 H L T V R P S K V I I D P R I L K V T T

10441 CAGAATGGTCTACGTCCCGACAGTTGAACAAAACCTGTCAGAGAAATGTTTTAGGAATGTG 10500
 T K G S A P S D V Q K S L R K V F D K C
 H R V L H L A T L K N Q C D R * L I R V
 D * W I C P Q * S T K V T E K C F G * V

10501 AGGTTTTATATGAAAACCATTACAATTTGGACCACCTTTGAAAATGACAAAATCGACGCAT 10560
 E L I Y K Q Y H * V Q H F K * Q K L Q T
 S W F I S K T I N F R T F S K S N * S R
 G F Y V K P L T L G P S V K V T K A A Y

10561 ATTACCGGCTGGTGTTCCTCGTAAAGTACAATGATACGCATCATCAATATGATAATTTCC 10620
 Y H G V V L P M E H * * A Y Y N Y * * L
 I I A S W L P C K M N S H T T T I S N F
 L P R G C P A N * T V I R L L * V I L P

10621 AAGAAAAACACACCCAGTACACCTAGACAACCAATACATAATTGTCCACTATCACAATT 10680
 N K K T H T M H I Q Q N H I L L H Y H *
 T R K Q T P * T S R N T I Y * C T I T N
 E K K H P D H P D T P * T N V P S L T L

10681 CAAACATATATACGTAGTTAATCTCGAGTCATGACCAACAGTGTGACCGTGACTAAAATG 10740
 T Q I Y A D I L A * Y Q N D C Q C Q N *
 L K Y I H M L * L E T S T T V S A S I K
 N T Y I C * N S S L V P Q * V P V S K V

10741 ACCATTAAAAATACCAGGTATATCTCTACGAGTTCAACATGTCAACGGTCAATTCCTGAT 10800
 Q Y N K H D M Y L H E L Q V T A L * P S
 S T I K I T W I S I S L N Y L Q W N L V
 P L K * P G Y L S A * T T C N G T L S *

FIG. 3 CONT'D

10801 GCAGGTCTGACAATTACAATAACGAACCGAGATACGTCGATATGAATTATTAACACGAAC 10860
R G S Q * H * Q K A R H L * V * Y N H K
V D L S N I N N S P E I C S Y K I I T S
T W V T L T I A Q S * A A I S L L Q A Q

10861 CAAACATGTTTACTACAAACAAGATGACTTCTAAAATTACAAACCGATACCGTTTACC, 10920
T Q V F H H K N * Q L N * H K P * P L H
P K Y L I I N T R S F I K I N P S H C I
N T C F S T Q E V S S K L T Q A I A F P

10921 AAAATCGGTTTCATTTTCGTCTAGAACAGAATCTACGAAACCGAAGTTACTGTCCACAAAG 10980
N * G L L L L D Q R L H K P K L S L H K
T K A L Y F C I K D * I S Q S * H C T N
K L W T F A S R T K S A K A E I V P T E

10981 ATAACCTTTGAAATAACCGACGATAATTGCGAGATATATACCCTAAAGTTCCAGCAGTTTA 11040
* Q F K I P Q * * A D I Y P I E L D D F
R N F S * Q S S N L T * I H S K L T T L
I S V K N A A I L R R Y I P N * P R * I

11041 TGATCCTTCAACATGAAAACTTCTACTTAACCGTGAAGACTGCAAATAGTTGTTAACCG 11100
V L F N Y K Q L H I P V K Q R K D V I P
Y * S T T S K F I F Q C R R V N I L L Q
S P L Q V K S S S N A G E S T * * C N A

11101 ACCACAATTTAACGTTAGATTTTGTGTTTTCTAAATAATTTCTTTGTTAAATAACCTAAAA 11160
Q H * I A I * F L F I * * L F L K N S K
S T N F Q L R F C F S K N F F C N I P N
P T L N C D L V F L N I L S V I * Q I K

11161 CTATAGATGTAAAAACAAATCAACATATTAAAGACGTAAACAATTTACCTGATATAAATA 11220
S I * M K T * N Y L K Q M Q * I S * I *
Q Y R C K Q K T T Y N R C K N F P S Y K
I D V N K N L Q I I E A N T L H V I N I

11221 CATATAATTATGTGTATACTAACCACAATGTAATACACATGAAACAAAACAATCAAAATA 11280
T Y * Y V Y S Q H * M I H V K N Q * N *
H I N I C M H N T N C * T Y K T K N T K
Y I L V C I I P T V N H T S Q K T L K I

11281 CTACAATGATCAATTTGTATTTCGTAAAAATAAACTGATACATATATTAAGGACATGAGAC 11340
S T V L * V Y A N K N S * T Y L E Q V R
H H * * N F M L M K I Q S H I Y N R Y E
I N S T L C L C K * K V I Y I I G T S Q

FIG. 3 CONT'D

11341 ATGGAACAAAATACATTTAATAAATCAACAAATATTCCTTCCAAAATCTCCAAAATGAAT 11400
Y R T K H L N N L Q K Y P L N * L N * K
T G Q K I Y I I * N N I L F T K S T K S
V K N * T F * K T T * L S P K L P K V *

11401 ACAGACCGAGAGTATAAAAACAAGGACGACACTTAAATGAATACAAATACTTCATAAAAT 11460
H R A R M N Q E Q Q S N * K H K H L I K
I D P E * I K N R S H I K S I N I F Y K
T Q S E Y K T G A T F K V * T * S T N *

11461 ACCAACATAAAATACACAAAACGATAAAAATATTGATACGTATCATAATTAGTACTGTA 11520
H N Y K I H K Q * K * L * A Y Y * D H C
I T T N * T N K S N K Y S H M T N I M V
P Q I K H T K A I K I V I C L I L * S M

11521 AAAAAGAACTACAAAAACCAACCATCTTATCAATGAAATTAAGATACACCATAAAACC 11580
K K K S T K P Q Y F L * K L K * T T N Q
N K R Q H K Q N T S Y N S * N R H P I K
K E K I N K T P L I T V K I E I H Y K P

11581 CAGCTTAAATCTTCTCCTACAAAACAATAAATAATGTCCGAAAAATCCATGAATATGTAC 11640
T S N L L P H K T I * * L R K L Y K Y M
P R I * F L I N Q * K N C G K * T S I C
D F K S S S T K N N I V A K K P V * V H

11641 CTGGTGATAAAACAGTAATCGATATCGTTTTTAAACAACGATTAACCAACAGACAATTATA 11700
S W * K T M L * L L F Q Q * N T T Q * Y
P G S N Q * * S Y C F N N S I P Q R N I
V V I K D N A I A F I T A L Q N D T L I

11701 TAAATAAAATGTCTACATGGAATATAATTTAACTAAGAGAACTCAATGAATAAATATCC 11760
I K N * L H V K Y * I S E R S N S I * L
Y K I K C I Y R I N F Q N E Q T V * K Y
N * K V S T G * I L N I R K L * K N I P

11761 CATATAAATAGAACAAATAACCCCTAAAAAGAGAGAAAATTTGTCACAAAATCTTACGG 11820
T Y K I K N N P I K R E K L C H K * F A
P I N * R T I P S K E R K * V T N K S H
Y I K D Q * Q P N K E R K F L T K L I G

11821 ATACCCACAAATATTAATATTTTAAAGACAAGTTCTTAACGCAATATACTTACGATTACC 11880
* P H K Y N Y F K Q E L I A N Y S H * H
R H T N I I I F N R N L F Q T I H I S I
I P T * L * L I E T * S N R * I F A L P

FIG. 3 CONT'D

11881 GAATGCAGGTGGAGCATTATCAAAACTCCGATAAAACAATTTAAATTTTGACGAACCTTA 11940
S V D V E Y Y N Q P * K T L N L V A Q F
A * T W R T I T K L S N Q * I * F Q K S
K R G G R L L K S A I K N F K F S S . P I

11941 TCCACCGCACGGTCAATAACTTCAGAGGTTTTAGTTAGTTTTAACTGACTACACTTTAC 12000
L H R A L * Q L R G F E I L I S Q H S I
Y T A H W N N F D G L N L * F Q S I H F
P P T G T I S T E W I * D F N V S T F H

12001 ACGATTACAACAAAACAATTTAACAATGTCGTAAACGTACAACGAAGATTAAGATTCAA 12060
H * H Q K T L N N V A N A H Q K * N * T
T S I N N Q * I T * L M Q M N S R I R L
A L T T K N F Q K C C K C T A E L E L N

12061 CACCGTCATAACATCACAAAATGTATTACTTTATGATAGATGAAGTCTAAACTCACATCG 12120
T A T N Y H K V Y H F V I * K L N S H L
Q P L I T T N * M I F Y * R S * I Q T Y
H C Y Q L T K C L S I S D V E S K L T A

12121 AAAACTATTCGAACGAGTTAATAACTAACAAAATAAGCGGTTAGGACGACGTCAACTATG 12180
K Q Y A Q E I I S Q K I R W D Q Q L Q Y
S K I L K S L * Q N N * E G I R S C N I
K S L S A * N N I T K N A L G A A T S V

12181 ATTCACAGAACGTTTCATATCTACTTCAATCGCTACTAATACAAGTTCTATCATGGCAAAA 12240
* T D Q L Y L H L * R H N H E L Y Y R K
S L T K C T Y I F N A I I I N L I T G N
L H R A L I S S T L S S * T * S L V T K

12241 CGTCCGAAACGTTTCACTCAAACATTTATACCGATCAAAACAACCTTATACTTCAGCGTTT 12300
A P K A F H T Q L Y P * N Q Q I H L R L
Q L S Q L T L K Y I H S T K N F I F D C
C A K C L S N T F I A L K T S Y S T A F

12301 CTTTTTAAACCGACTACGATTTTTATCACCAAGACAATTAGTTGTTGTCTATTTTGTCAA 12360
S F N P Q H * F Y H N Q * D V V S L V T
L F I Q S I S F I T T R N I L L L Y F L
F F K A S A L F L P E T L * C C I F C N

12361 TCTTTTTCGTACATTATATCGATTGACACATACTTGCACTATTTGACATCGAGCGTT 12420
L F L M Y Y L * T Q T H V H Y L Q L E C
* F F C T I Y S L R H I F T I F S Y S A
S F A H L I A L D T Y S R S L A T A R L

FIG. 3 CONT'D

12421 TGAACCTGTCATACCGTCTGGATCGTGAATGATTGTACATATTTCTCCGAGCCTAATTACT 12480
V Q V Y P L G L V * * C T Y L P E S * H
F K F T H C V * C K S V H I F L S P N I
S S R I A S R A S V L M Y L S A R I L S

12481 ATTCTTCTCATTTCAACAAAGGCGAAACGTCTGTTACGAAAAATCGTACCAAGCATTAA 12540
Y S S Y L Q K R K A S L A K * C P E Y I
I L L T F N N G S Q L C H K K A H N T F
L F L L T T E A K C V I S K L M T R L N

12541 CCTATTAGTCCGAAATTTAAGATAAGACCTATTACGACAATTTCCAACACATGGAAACTC 12600
P Y D P K L N * E P Y H Q * L N H V K S
Q I I L S * I R N Q I I S N F T T Y R Q
S L * A K F E I R S L A T L P Q T G K L

12601 ACGATAAGGTCGTAACCGACGATTATGAAATTGATATCATTATGGTCTATTTGTTCAAAA 12660
H * E L M P Q * Y K L * L L V L Y V L K
T S N W C Q S S I S * S Y Y Y W I F L N
A I G A N A A L V K V I T I G S L C T K

12661 ACTATTTCAACAACATATTACAAATACAATGTATACGACCATCACATACCGTATATGTCTG 12720
Q Y L Q Q Y H K H * M H Q Y H I A Y V S
K I F N N I I N I N C I S T T Y P M Y L
S L T T S L T * T V Y A P L T H C I C V

12721 ACAAGTTCTACGACTACCATAATTATTTGTCAATTGACTATAATCACAACCTAAGATTAAC 12780
Q E L H Q H Y * Y V T L Q Y * H Q N * N
S N L I S I T N I F L * S I N T N I R I
T * S A S P I L L C N V S I L T S E L Q

12781 CGGAGAACAATAGTAACGCTTGTCCATATTACTTCAACGATTACGACAATACGTCTTATT 12840
A E Q * * Q S C T Y H L Q * H Q * A S Y
P R K N D N R V P I I F N S I S N H L I
G R T I M A F L Y L S T A L A T I C F L

12841 ACTCAACTACGGAGTATTTAATTTTATGTTCAACAATTATCACCAAGACTATACTTAAC 12900
H T S A E Y I L F V L Q * Y H N Q Y S N
I L Q H R M F * F Y L N N I T T R I H I
S N I G * L N F I C T T L L P E S I F Q

12901 ATTATAAGGATGAGTTACAATAATATTATTACCATCATCACCATCTTATCAAATACGACA 12960
Y Y E * E I N N Y Y H Y Y H Y F L K H Q
T I N R S L T I I I I T T T T S Y N I S
L I G V * H * * L L P L L P L I T * A T

FIG. 3 CONT'D

12961 AGAATCACTACAACCTACCAGAATTCATATGATTCTATTACTTTCTACTACCTTTAACACA 13020
E * H H Q H D * T Y * S L S L H H F N H
N K T I N I T K L I S L Y H F I I S I T
R L S T S P R L Y V L I I F S S P F Q T

13021 ACAAATCTCGAACTAGGAGGAACATTAAAGATATGTTCTACAATTCCTGAATTTTA 13080
Q K L A Q D E K Y I K * V L H * P V * F
N N * L K I R R T F K R Y L I N L S K F
T K S S S G G Q L N E I C S T L P S L I

13081 ATTATAGAAATAAAATAATTTCTACATTGTGAAATCGATCTCCACCCAACAACCATG 13140
* T D K N * * L I Y C K L * L T P Q Q Y
N L I K I K N F S T V S * S S P P N N T
L Y R * K I L P H L V K A L P H T T P V

13141 AAATAGAAGTTGTTAATCTAACGTCGACCACAACGATGACTCATACGTCGATTAAGAAG 13200
K I K L L * I A P Q H Q * Q T H L * N K
S * R * C N S Q L S T N S S L I C S I R
K D E V I L N C A P T A V S Y A A L E E

13201 ATATGAAAGTAATACACGTAAAAGACATCTAGGATTCTTTTGAATAAATCTAATATATGT 13260
* V K M I H M K Q L D * S F K N L N Y V
R Y K * * T C K R Y I R L F S I * I I Y
I S E N H A N E T S G L F V * K S * I C

13261 TGTTCCACCACATGGATATTAATTAACAÇAATTTTACGAGACACTAGTACGACCATGACC 13320
V L H H V * L * N H * F A R H D H Q Y Q
L L T T Y R Y N I T N F H E T I M S T S
C P P T G I I L Q T L I S Q S * A P V P

13321 ATACCGGTAATGATAAATTTGGACTCCGATGATAATTGGTTCTAAGAATACCACCACGGAG 13380
Y P W * * * V Q P * * * G L N K H H H R
T H G N S N F R L S S N V L I R I T T G
I A M V I L G S A V I L W S E * P P A E

13381 TCAAACATAAATAACGGCACGTGCACATCTCGTAGGTCTACATCTACCATATACATTTAA 13440
L K Y K N G H V H L A D L H L H Y I Y I
* N T N I A T C T Y L M W I Y I T Y T F
T Q I * Q R A R T S C G S T S P I H L N

13441 TGCACCATTTAAACATGTTTCAGGGAACCCATATTTTCTAGGATAAGAAATACACAATTG 13500
V H Y I Q V L G K P Y L L D * E K H T L
* T T F K Y L D R Q T Y F I R N K I H *
R P L N T C T G K P I F S G I R * T N V

FIG. 3 CONT'D

13501 TGTACTACAAACAGTTCAGACACCAAAAACCTCTCTACCGTCAACAAGGACACATCCAAG 13560
V H H K D L R H N K S L H C N N R H L N
C M I N T L D T T K P S I A T T G T Y T
C S T Q * T Q P K Q L S P L Q E Q T P E

13561 TTCACAGCGACAAGTTAGATTCTCTAAATTTAAAAAATTGCCCCAAGCCCCATGATCACAC 13620
L H R Q E I * L N L N K L R T R P V L T
* T D S N L R F I * I K * V P E P Y * H
L T A T * D L S K F K K F P N P T S T H

13621 TTACGGGCCGATCATGGGACACGATCACCAAATAGATGACTACAAGTTAATTCCTCGTAA 13680
F A R S T G Q A L P K D V S T * N L A N
S H G A L V R H * H N I * Q H E I L P M
I G P * Y G T S T T * R S I N L * P C K

13681 CTGTAAACATTATGGTTATCTCGACCATATCCAAATATAATATTTCACTTAACAACGGCA 13740
S M Q L V L L A P I P K Y * L T F Q Q R
Q C K Y Y W Y L Q Y L N I N Y L S N N G
V N T I G I S S T Y T * I I F H I T A T

13741 AAAGTCGCATATCTACTGCTGCCATTATTTAACCTATTCAAGAAACAACAGTTTCTTGA 13800
K * R I S S S P L L N S L N K T T L L V
N E A Y L H R R Y Y I P Y T R Q Q * P F
K L T Y I V V T I F Q I L E K N D F S S

13801 TTAAATCTTCAAATATTATTTCTCTTTTGAATAATACTCAACTGATTTTCAACACCACAA 13860
L K S T * L L S F V * * S N V L L Q P T
* N L L K Y Y L S F K N H T S * F N H H
I * F N I I F L F S I I L Q S F T T T N

13861 CACCGACTTGTACTAAAGAAATGTAAACTATAACTACCATCAGCGCACGGTGTATATCAA 13920
T A S C S K K V N S I S P L R T G C I T
Q P Q V H N R * M Q Y Q H Y D R A V Y L
H S F M I E K C K I N I T T A H W M Y N

13921 GCATCCTTAGAAAGTTTCATATGATACAATCTAGAAACGATACGTAACGCAGTAAACTA 13980
R L F R E F Y V I N S R Q * A N R * K S
E Y S D K L T Y * T L D K S H M A D N Q
T P I K * L I S H * I K A I C Q T M K I

13981 GCATTACTAACAAGTTATAACACACTTTAAGAAACACTCATACGACTAACATTTCTTAGG 14040
R L S Q E I N H S I R Q S Y A S Q L S D
D Y H N N L I T H F E K H T H Q N Y L I
T I I T * Y Q T F N K T L I S I T F F G

FIG. 3 CONT'D

14041 ATGAAAAGATTCTTTCTAACCATACTAAAACAACTTTTAGGACTATAATAATTATATATA 14100
 * K E L F S Q Y S K T S F G S I I L I Y
 R S K * S L N T H N Q Q F D Q Y * * Y I
 V K R L F I P I I K N F I R I N N I Y I

14101 TTTTAAATCCGGGATAAAAATTATCTCGAAATGAATTATGACAGTAAAAACGTCTGTGG 14160
 L F N P G I K L L A K S L V T M K A S V
 Y F I L G * K * Y L K V * Y Q * K Q L C
 F F * A R N K I S S * K I S D N K C V G

14161 AATCAACTTCATCCAAATCAACCACAAAATTGAAATCTATTGGTTCTAAACATACCAGTT 14220
 K T S T P K T P T K V K S L W S K Y P *
 R L Q L L N L Q H K L K L Y G L N T H D
 * N F Y T * N T N * S * I V L I Q I T L

14221 ACCATACTAAAACCACTAAAATATGTTTGTGGGGTCCCAAACCAACCGTCAACGTCTA 14280
 H Y S K P S K I C V A G P N P T A T A S
 I T H N Q H N * V F L G L T Q H P L Q L
 P I I K T I K Y L C G W P K T H C N C I

14281 AGAATGATAAGAATATACTACGGATACAACCTGATACACAGTACATAATCTAACACTTAAT 14340
 E * * E * I I G I N V I H * T N S Q S N
 N K S N K Y S A * T S * T D H I L N H I
 R V I R I H H R H Q S H T M Y * I T F *

14341 AAACAATTACTATCAATATCTGTTAAGCTAGAACATGTCATACTAAAATGACTAATGTTTC 14400
 N T L S L * L C N S R T C Y S K V S * L
 I Q * H Y N Y V I R D Q V T H N * Q N C
 K N I I T I S L E I K Y L I I K S I V L

14401 AATCTCAACAAATTATTCATAAAATTCATAACCCCATACTTCATAGTAGGATTATGACAC 14460
 N S N N L L Y K L Y Q P I F Y * G L V T
 T L T T * Y T N * T N P Y S T D D * Y Q
 * L Q K I L I K L I P T H L I M R I S H

14461 CTAACACTATTACTATCCACATAATAAGTAACACGATTAAAATTATATGATAAATCATAC 14520
 S Q S L S L H I I * Q A L K L I S N L I
 P N H Y H Y T Y * E N H * N * Y V I * Y
 I T I I I P T N N M T S I K I Y * K T H

14521 CAAAATGGATTATGAACAAAACAGGGGAACAATCTGTTTAAAAACATCTACCACATGGC 14580
 T K G L V Q K P G R T L C I K T S P T G
 P K V * Y K N Q D G Q * V F K Q L H H V
 N * R I S T K T G K N S L N K Y I T Y R

FIG. 3 CONT'D

14581 AAACAACAAAGATAACCAATGGTAATGTTTCTCAATCCACATCAATACTTGAATCTACAA 14640
 N T T E I P * W * L S N P T T I F K S T
 T Q Q K * Q N G N C L T L H L * S S L H
 K N N R N T V M V F L * T Y N H V * I N

14641 CTGTGTGTGGCAATAGCAAACAGAGAATTTCTAAATGAAGAAATACGTCGTCTAGGACGA 14700
 S V C R * R K D R L S K S R * A A S G A
 Q C V G N D N T E * L N V E K H L L D Q
 V C V T I T Q R K F I * K K I C C I R S

14701 TACGTGCAACGTAGACGATCACGAGACGAACTAAATGCTTGAACAACAAAATCACATCGA 14760
 I C T A D A L A R S S K R V Q Q K L T A
 * A R Q M Q * H E A Q N V F K N N * H L
 H V N C R S T S Q K I * S S T T K T Y S

14761 CGGTAATGTTACCATATTTTAAAGTTTGACATTTTGGTCCATTGAAATTGGTTCTGAAA 14820
 A M V L P I F N * V T F G P L K L W S K
 Q W * L H Y L I E F Q L V L Y S * G L S
 G N C T T Y F K L S Y F W T V K V L V K

14821 ATGCTCAACAATTTTCATTTCCGAACAAATTTCTCCCATCATGTCAACTAAACTTTGTA 14880
 * S N T L L L P K N L S P L V T S K F C
 K R T Q * F Y L S T * L P Y Y L Q N S V
 V L K N F T F A Q K F L T T C N I Q F M

14881 AAAAAGAAATGAGTTCTACCATTACGACGTTAATGACTAATATTAATAATATTCATATTA 14940
 K K K V * S P L A A I V S * L * * L Y L
 N K R * E L H Y H Q L * Q N Y N N Y T Y
 K E K S L I T I S C N S I I I I I I L I I

14941 AATGGATGATACCAACTATAATTTCGTCAATAACAAACATAATCTTCAACAAATATTATA 15000
 K G V I T S I L C N N N T N S T T * L Y
 N V * * P Q Y * A T I T Q I L L Q K Y I
 * R S H N I N L L * Q K Y * P N N I F I

15001 AAACTTTAAATACTACCACCAACATATGGTCGTAGTGTCAATAACAATTATTAATACTA 15060
 K S I * S P P Q I G A D C T I T L L * S
 N Q F K H H H N Y V L M V L * Q * Y N H
 K F N I I T T T Y W C * L N N N I I I I

15061 TTTTCACGACCAATAGGTAAATTATTTAAACCATTTTCGGTCTGAAATAATACTCCGTAAT 15120
 L L A P * G N L L N P L A L S * * S A N
 Y F H Q N D M * Y I Q Y L W V K N H P M
 F T S T I W K I F K T F G S K I I L C *

FIG. 3 CONT'D

15121 AGTAAACTCCTTGTCTTACTTTAAATACGTATATGATTGTCATTACAAGACGGGTGGAAT 15180
D N S S C F S I * A Y V L R L T R G V K
I M Q P V S H F K H M Y * V Y H E A W R
* K L F L I F N I C I S F T I N Q G G *

15181 TGAGTTTACTTAAATTTTATACGATAGTCACGATTCTTATCTCGAGCGTGACATCGTCCA 15240
V * I P K F Y A I L A L F L A R V T A P
L E F S N L I H * * H * S Y L E C Q L L
S L H I * F I S D T S L I S S A S Y C T

15241 CAAAGATAAGAATCATGATACTGTCCGGCTTACAAGGTAGTTTTTACAACTTCTCATAT 15300
T E I R L V I V P R I N W * F H K F L I
H K * E * Y * S L G F T G D F I N S S Y
N R N K T S H C A S H E M L F T Q L T Y

15301 CGTCGATGGGCTCCACAAGGACAACAATATCCTTGGTGATTTAAATACCACCAACCCCTG 15360
A A V R P T G T T I P V V L N * P P Q S
L L * G L H E Q Q * L F W * I K H H N P
C S G S T N R N N Y S G S F K I T T P V

15361 CTATACAATGCAGTAGAATATTTCTACAACCTGTTGGCACAAGAATACCCAACCCTAATA 15420
S I N R * R I F S T S L G T R I P Q S *
R Y T V D D * L P H Q C G Q E * P N P N
I H * T M K Y L I N V V R N K H T P I I

15421 GGATTTACACTAGCACGATACGGTTTATAAAACGCATAACAATCATCAAATCAAAACCGG 15480
G L H S R A I G F I K R I T L L K T K A
D * I H D H * A L Y K A Y Q * Y N L K P
R F T I T S H W I N Q T N N T T * N Q G

15481 GCGTTTGTACTTAAACAACAAGTGTAACCACTATCTAAAATAGCGGAACGCTTACTTACA 15540
R L C S N Q Q E C P S L N * R R A F S H
G C V H I K N N V H H Y I K D G Q S H I
A F M F K T T * M T I S K I A K R I F T

15541 CGAGTTCAAAACTCACTTTATCAATACACACCGCCAACGATAATACAATTCGGACCACCA 15600
A * T K L S I T I H P P Q * * T L G P P
H E L K S H F L * T H R N S N H * A Q H
S L N Q T F Y N H T A T A I I N L R T T

15601 TGATCGTCACCACTACGTTGATGACGAAAACGATTAAGACAAAAATTATATACAGTCCGA 15660
V L L P S A V V A K A L E T K L I H * A
Y * C H H H L * Q K Q * N Q K * Y I D P
S A T T I C S S S K S I R N K I Y T L S

FIG. 3 CONT'D

15661 CAATGACGATTACAAACAAGAGAATACCGGACATTACCGGTATTCTAACTTCTAAATTCA 15720
T V A L T Q E R I A Q L P W L I S S K L
Q * Q * H K N E * P R Y H G Y S Q L N L
N S S I N T R K H G T I A M L N F I * T

15721 TATGCGTTAAATGTTTTGCGAATATGAGATTACAAATAGCATGTCTAATACAATAA 15780
I R L K C F R K Y E L T * R V S * T S *
Y V C N V F V S I S * H K D Y L N H Q N
Y A I * L F A * V R I N I T C I I N I I

15781 TGTAAACAATTACTCATAATACTTAAAAATACATTCGTAAAATCATACTACTAAAACTCA 15840
V N T L S Y * S N K H L C K L I I I K L
Y M Q * H T N H I K I Y A N * Y S S K S
C K N I L I I F K * T L M K T H H N Q T

15841 CTACTACCACAACAGACAATATTGAGACTAATACGATCATTCCCAATATATCGATTATAT 15900
S S P T T Q * L E S * A L L P * I A L I
H H H H Q R N Y S Q N H * Y P N Y L * Y
I I T N D T I V R I I S T L T I Y S I Y

15901 TCACAAAAAGTTGTTCAAAACATGATAGTCTTATTACAGAAATACAGACTTAGATTTACA 15960
L T K * C T K Y * * F L T K I D S D L H
L H K E V L K T S D S Y H R * T Q I * I
T N K L L N Q V I L I I D K H R F R F T

15961 ACCCAACTTTTACTATAATGATTACCAGGAGTACTTAAACAAGGGTTGTATGATACAAT 16020
Q T S F S I V L P G * S N Q E W C V I N
N P Q F H Y * * H D E H I K N G V Y * T
P N F I I N S I T R M F K T G L M S H *

16021 CAATTCTATCTACCACTAATAACAATAAATGGTATAGGTCTAGGAAGATCTTAAATCCT 16080
T L I S P S * T * K G Y G S G E L I K P
L * S L H H N H K N V M D L D K * F K L
N L Y I T I I N I * W I W I R R S N * S

16081 CGACCAACAAAACAATACTTCTGACTGTCACAAGAAAATCTCTCGCGAAA 16140
A P Q K T S S K N F V S L T R K I S R K
L Q N N Q Q H N I S S Q C H E K S L A S
S T T K N I I * Q L S V T N K Q Y L A K

16141 CATTCAGATCGATATCTACGAATGGGAAATCATGTAGTACTTTTACTTCTTATGGTTTT 16200
T L R A I S A * G K T C * S F S S Y W F
Q L D L * L H K G K L V D H F H L I G F
Y T * S Y I S V R * Y M M F I F F V L F

FIG. 3 CONT'D

16201 CAGAAAGCACATATAAATCTTATATATTTTTTTTGACATATTACTAGAACCATGAGTCTAG 16260
T K R T Y K S Y I F F S Y L S R P V * I
L R E H I N L I Y L F V T Y H D Q Y E S
D K T Y I * F I Y F F Q I I I K T S L D

16261 AATCTATCAATATCACATAAAATTCATGAACACTACCAAATTTCAAATGACTTCTTAGT 16320
K S L * L T I K L V Q S P K F N V S S D
R L Y N Y H * K L Y K H H N L T * Q L I
* I T I T N N * T S T I T * L K S F F *

16321 AAAATGTTCTTATACATAAATTTTTTCACGGCACTACGTCTCACATCCACGTACGCAACAA 16380
N * L F I Y K F L A T I C L T P A H T T
M K C S Y T N L F H R S A S H L H M R Q
K V L I H I * F T G H H L T Y T C A N N

16381 ACAAGTAGTGTTTGAAGAAACGCAACACCGTCAACATATGCATTTCGGAACAATACAACA 16440
Q E D C V E K R Q P L Q I R L G K N H Q
K N M V F K K A N H C N Y V Y A K T I N
T * * L S R Q T T A T T Y T L R Q * T T

16441 TTTACAACAATACTGGTACAATACCGTTGATTAGTATTTTATACAAAACCTCACAGAGTGGA 16500
L H Q * S W T I A V L * L Y T K L T E G
Y I N N H G H * P L * D Y I H K S H R V
F T T I V M N H C S I M F I N Q T D * R

16501 ATGCAAAACATTACGTGGATTGACACTACACTCACTACAGTGGTTTAAATATAAACCCGCCA 16560
* T Q L A G L Q S T L S T V L N Y K P P
K R K Y H V * S H H S H H * W I I N P R
V N T I C R V T I H T I D G F * I Q A T

16561 TACAGAATGATAAACTTTTGGTATTTGGGGTAATAAGTAAATTCAATCAATACTTACCA 16620
I D * * Q S F W L G W * E N L N T I F P
Y T K S N H F G Y V G N N M * T L * S H
H R V I T F V M F G M I * K L * N H I T

16621 TACCAGAAACCAAACATATTTGTTAGAACGTGCCCAAGTGAATATATCTACTAAAATTA 16680
I T K P K Y L C D Q V P E G * I S S K L
Y P R Q N T Y V I K C P N V K Y L H N *
H D K T Q I F L R A R T * R I Y I I K I

16681 TTCTATCGATCAACATTTACCTGTCTTCAACTACTAATACAAGACCGTTTACTCACATAA 16740
L I A L Q L H V S T S S * T R A F S H I
Y S L * N Y I S L L Q H N H E P L H T Y
L Y S T T F P C F N I I I N Q C I L T N

FIG. 3 CONT'D

16741 CTTGCAAATTTCAATAAACGACGTCTTTGAGTTTTCCGTTGACTTCTCCGAAAATTTGTT 16800
S R K F N N A A S V * F A V S S A K L C
Q V N L T I Q Q L F E F P L Q L P K * V
F T * L * K S C F S L L C S F L S K F L

16801 TCGATACGAAGACGATGGTAAGTTCTCTAACAATCACTATCTCTTCAATAAACACAACC 16860
L * A E A V M * S I T L S L S T I K H Q
F S H K Q * W E L S Q * H Y L L * K T N
A I S R S G N L L N N T I S F N N Q T P

16861 CTCTGTCCATTTC AATTTGGTGGTGAATTATTTTAAATACAAAAGTGTCGGATGGTAAAA 16920
S V P L T L G G S L L F * T K V P * W K
P S L Y L * V V V * Y F N H K * L S G N
L C T F N F W W K I F I I N E C A V M K

16921 TGATCATGACCATTCTGTCAAAATCCACTCATACAAAACACTATTTTCACTTAATTGATTG 16980
V L V P L V T K P S Y T K S L L S N V L
* * Y Q Y S L K L H T H K Q Y F H I L *
S T S T L C N * T L I N K I F T F * S V

16981 CCACACATAATGGCGCGATGTTGATGAATATTTGAAAGATATCCACTACAAAACAAAAT 17040
P T Y * R A V V V * L S E I P S T K T K
R H T N G R * L * K Y V K * L H H K Q K
T H I V A S C S S I F K R Y T I N K N *

17041 TGTAGTGTAAGACATCGATCAAATTCACGTGGATGTGAACAGGGTGTCTCTTGATACGA 17100
V D C E T A L K L A G V S T G C S F * A
L M V N Q L * N L H V * V Q G V L S S H
C * M R Y S T * T C R C K D W L L V I S

17101 TCATATTCTAAAAGATCACAATATCACAAGGTAACCACAAAGTTTTATTACAACGATTA 17160
L I L N E L T * L T G N T N * F L T A L
* Y L I K * H K Y H E M P T E F Y H Q *
T Y S K R T N I T N W Q H K L I I N S I

17161 ATAGTCGTGTAACCTTACTTTGCAATAACGTGACAAGTTCCAGGGGGACCATGCCCTTTC 17220
* * C M P I F R * Q V T * P G G P V P F
N D A C Q F S V N N C Q E L D G Q Y P F
I L V N S H F T I A S N L T G R T R S L

17221 AGAGTAGAACGATATCCAGATCGACAAATAATGATGTGTCGTGCACATCAAATATGACGA 17280
D * R A I P R A T * * * V A R T T * V A
T E D Q * L D L Q K N S C L V H L K Y Q
R M K S Y T * S N I V V C C T Y N I S S

FIG. 3 CONT'D

17281 CGATCAGTACGACGACATCTACGTAACACACTTTTTCGAATATTCAAAAATTATAATTG 17340
A L * A A T S A N H S F A * L N K F I L
Q * D H Q Q L H M T H F L K Y T K L Y *
S T M S S Y I C Q T F F S I L K * I N V

17341 CTAACATGTGCATAATAAGGACGATTTCAAGCACATCTAACAATACTATTCAAATTTTAA 17400
S Q V R I I G A L T R T S Q * S L N L I
R N Y V Y * E Q * L E H L N N H Y T * F
I T C T N N R S F N T Y I T I I L K F N

17401 TTACTATGGTGAACATTTCATACAAAATGGTGTTATTTACGTAATGGTCTCAACCAATGT 17460
L S V V Q L Y T K V V I F A N G S N T V
* H Y W K Y T H K * W L L H M V L T P *
I I G S T L I N K G C Y I C * W L Q N C

17461 CTATAACAACAACAATACTTCAATCATACGAATGATTAATACTTAACAGACAATATTTA 17520
S I T T T S S T L I S V L * S N D T I F
L Y Q Q Q Q H L * Y A * * N H I T Q * L
I N N N N I F N T H K S I I F Q R N Y I

17521 CGAGCATAATTTGATTTGTAATACATATATAACCTCTAGGACGAGTTAATGGACGTGGT 17580
A R I L A L C * T Y I P S G A * N G A G
H E Y * L * V N H I Y Q L D Q E I V Q V
S T N F S F M I Y I N S I R S L * R C W

17581 GCACACGACAACCTCGTTCCCAAGAAATCTTGGATCCGTGAAGTTAAGATAATGATTTTAT 17640
R T S N L L P E K S G L C K L E I V L I
V H A T S C P N K L V * A S * N * * * F
T H Q Q A L T R * F R P V E I R N S F Y

17641 TACACAACAAATCCAGGACTATAGAAAAACCCTTTAACAATATCCACAGGATTTCTTTAA 17700
I H Q K P G S I K K P F Q * L H G L S I
L T N N L D Q Y R K P F N N Y T D * L F
H T T * T R I D K Q S I T I P T R F F N

17701 CATCTTTGACAAAGTCGTAACCAATACTATTATTTGAGTTCCGATTTTACTATTATCA 17760
T S V T E A N T * S L L S L A L F S L L
Q L F Q K L M P K H Y Y V * P * F H Y Y
Y F S N * C Q N I I I F E L S F I I I T

17761 AGTAATACAAAATTTTCATATAAAATCCCTGTCTGTGTGTACTCTCAAGTTCACGACAT 17820
E N H K L T Y K L P C V V C S L E L A T
N M I N * L I N * P V S L V H S N L H Q
* * T K F Y I K L S L C C M L T * T S Y

FIG. 3 CONT'D

17821 TTATAAGTTGTCTATATAGATTAAATCATTTAAAAATTTTCGATTAGGTCAAACCTTATCA 17880
 F I * C I Y R I L L N K F A L G T Q F L
 L Y E V S I D L * Y I K L L * D L K S Y
 I N L L Y I * N T F K * F S I W N P I T

17881 CGACAAAAATAATCAGGAATATTATCAGTCTTAATACAACGATTGCGACAAAATCCACAA 17940
 A T K I L G * L L * F * T A L R T K P T
 H Q K * * D K Y Y D S N H Q * A H K L H
 S N K N T R I I T L I I N S L T N * T N

17941 GTTTGTGTTTGACATCTAAGACGAGTTCCAAGCCTTATACTAATACAATATATAAGTGTT 18000
 * V C V T S E A * P E S Y S * T I Y E C
 E F V F Q L N Q E L N P I H N H * I N V
 L C L S Y I R S L T R F I I I N Y I * L

18001 TGTCGTCTTTGTCGGGTAAGACAATTACAATTAGCTAAATTACAACGGTATTGATCTCGG 18060
 V A S V A W E T L T L R N L T A M V L A
 F L L F L G N Q * H * D I * H Q W L * L
 C C F C G M R N I N I S K I N G Y S S G

18061 TTCTTCCCGTAAAAAACACAATACTCATTATACGTTAATAAACTTAGAGAATTAAAATAA 18120
 L F P M K Q T I L L I C N N S D R L K I
 W S P C K K H * S Y Y A I I Q I E * N *
 L L A N K T N H T I H L * K F R K I K N

18121 TGAGATGGAAATCTATTTTAAGTTTGTAGTTGAAATGGAGCAAACGTAACGTGTTGATTA 18180
 V R G K S L I * F * V K G R K C Q V V L
 * E V K L Y F E F D F K V E N A N C L *
 S * R * I F N L I L S * R T Q M A C S I

18181 GAAAAATTCTAACATCATTTTCAACGAATCCAATAGTAGGTGCGGTACGGGGGAGTAAA 18240
 R K L S Q L L L Q K P * * G A C A G E N
 D K * L N Y Y F N S L N D D L A H G R M
 K K F I T T F T A * T I M W R M G G * K

18241 AATCGTCAACTACTATTTATATTCCAATTACTTTTAAACCGACATTTAAATTTATAAACA 18300
 K A T S S L Y L T L S F K A T F K F I Q
 K L L Q H Y I Y P * H F N P Q L N L Y K
 * C N I I F I L N I F I Q S Y I * I N T

18301 CTTGGACAAAATTGTATAAGAGCAAATTATAGAGAATACCCAAAATTTAATCTAAACTGA 18360
 S G T K V Y E R K I D R I P K L N S K V
 H V Q K L M N E N L I E * P N * I L N S
 F R N * C I R T * Y R K H T K F * I Q S

FIG. 3 CONT'D

18361 GAACTACCAATAAGATTTAACAAATAATGATTTCTACTTCGGTAATTTGCACAATCTCCA 18420
R S P * E L N N I V L S S A M L R T L P
E Q H N N * I T * * * L H L W * V H * L
K I T I R F Q K N S F I F G N F T N S T

18421 ACCCAACCAAACTACAACCTCCCGCGAGTACGATGAGCGCTTTTGTAACCTTGTGTTGAAA 18480
Q T P K S T S P A * A V R S F M P V F K
N P Q N Q H Q P R E H * E R F C Q F L S
P N T K I N L A S M S S A F V N S C V K

18481 GGTGACGTTTATCCAAAAAGTTGACCACACCTAAAACATCAACTTCGATGACCGAATAAA 18540
G S C I P K E V P T S K T T S A V P K N
E V A F L N K L Q H P N Q L Q L * Q S I
W Q L Y T K * S T H I K Y N F S S A * K

18541 CGACTCTCTCTAACAATATGAAAATTTTTTTGACATCGATTTCGAGGAGGACCACTTTTT 18600
A S L S Q * V K L F V T A L A G G P S F
Q Q S L N N Y K * F F Q L * L E E Q H F
S L S I T I S K F F S Y S F S R R T F F

18601 AAATTTGTAAATTATGGGGAATACAGTTTTCCAGTTTTCCACCTATAACAATCTTAATCT 18660
N L C K I G R I D F P * F H S I T L I L
I * V N L V G * T L L D F T P Y Q * F *
K F M * Y G K H * F T L L P I N N S N S

18661 TAACAAGTTTACAATAGACTAATAGAAAATCTGGAAAGACTATCACATCATAAATAATGA 18720
I T * I N D S * R K S R E S L T T N I V
F Q E F T I Q N D K L G K Q Y H L I * *
N N L H * R I I K * V K R I T Y Y K N S

18721 ACCAGACGGTCAAAACTTGAATGAACAAATTCATATAAACGATTTAATCCGTCTCTCGAA 18780
Q D A L K S S V Q K L Y K A L N P L S S
K T Q W N Q V * K N L T N Q * I L C L A
P R G T K F K S T * P I K S F * A S L K

18781 TTAACATTACACACAAGATTAGCACGATGTACGATGTTAAGATCTTGACCAATAATACCA 18840
L Q L T H E L R A V H * L E L V P * * P
* N Y H T N * D H * M S C N * F Q N N H
I T I H T R I T S C A V I R S S T I I T

18841 ACAACCGCGGTATCAATATGAACACTAATACACATATTAGGTGAATAACATCTATATGTT 18900
Q Q R W L * V Q S * T Y L G S I T S I C
N N A G Y N Y K H N H T Y D V * Q L Y V
T P A M T I S T I I H I I W K N Y I Y L

FIG. 3 CONT'D

18901 GTCACCCCAATATGTCCAAGAAATTGATCATTAGTGCTATATTAACATTACATGTATTT 18960
C H P * V P E K V L L * S I I Q L T C L
V T P N Y L N K L * Y D R Y L K Y H V Y
L P T I C T R * S T I V I Y N T I Y M F

18961 CCACGTGTACAACGCAGTCGACTACGTTAATACTGAGCAACAAATCGTTAGATACTAACA 19020
P A C T A D A S A I I V R Q K A I * S Q
L H V H Q T L Q H L * S E N N L L R H N
T C M N R * S I C N H S T T * C D I I T

19021 AAAACATTTAGACAATTAACCTTAAATCTCATAGGTTAFTAAAGATTACTCCAGTCATAT 19080
K Q L D T L Q F K S Y G I I E L S T L I
N K Y I Q * N S N L T D L L K * H P * Y
K T F R N I P I * L I W Y N R I L D T Y

19081 TTATGTAGAACATCCAATAACGTCGCACAGTACGAATTTGACGGTACGATACATTATCT 19140
F V D Q L N N C R T M S L A A M S H L L
L Y M K Y T I A A H * A * L Q W A I Y Y
I C R T P * Q L T D H K F S G H * T I S

19141 ATGTTGAATACAATACTGTATCCGTTAGGATTTCCAAATCGAACACAGTTTCTAATACTT 19200
Y L K H * S M P L G L P K A Q T L S * S
I C S I N H C L C D * L N L K H * L N H
V V * T I V Y A I R F T * S T D F I I F

19201 AAATTTAAAATACTACGAAAAGGACATCGGTTGAGACAATTTGTCAATAAAATACAGATA 19260
N L N * S A K G T A L D T L C N N * T *
I * I K H H K E Q L W T Q * V T I K H R
K F K I I S K R Y G L R N F L * K I D I

19261 CTACACGTATTTCTATTAATAATTTCTACCAAATACATACAAAACCTTAACATTACAATA 19320
S T C L S L K L S P K H I N Q F Q L T S
H H A Y L Y N * L H N I Y T K S N Y H Q
I H M F I I K F I T * T H K P I T I N I

19321 TTTATAGGTAGATTAAGTTAACAACATCTAAACTGTGAGCTCACAATTTATTTAATTTG 19380
L Y G D L E I T Q L N S V R T N F L N F
Y I D M * N L Q K Y I Q C E L T L Y I L
F I W R I * N N T S K V S S H * I F * V

19381 GAAGGACCTACATTACCACCATCAAACATACAATTATTTGTACGTAAGGTATGATTAGGA 19440
R G P H L P P L K Y T L L C A N W V L G
G E Q I Y H H Y N T H * Y V H M G Y * D
K R S T I T T T Q I N I F M C E M S I R

FIG. 3 CONT'D

19441 AAATGATCTTGACAAAACTTTTAGAATTCGGATACGGAAAAAGATAATAAGTCTATGC 19500
K V L V T K S F R L G I G K K * * E S V
K * * F Q K Q F D * A * A K K R N N L Y
K S S S N K F I K L R H R K E I I * I R

19501 GGAACACACATGCATCTACCAAATCTTAGATTTGTTCAACTAATGCAAGGAAATCTTCG 19560
G Q T Y T S P K S D L C T S * T G K L L
A K H T R L H N L I * V L Q N R E K L F
R T H V Y I T * F R F L N I V N R * S A

19561 CGGTGAACATAGTGTGCCACATTAGATCCACCTCGACAAACAAGTTTCGTACGACTTCTT 19620
A V Q I V R H L R P P A T Q E F C A S S
R W K Y * V T Y D L H L Q K N L A H Q L
G S T D C P T I * T S S N T * L M S F F

19621 ATAACATTGATGGAACCTCAGAATATTATATCAATGATGTCGTCGAAATGAAAAACCCAA 19680
Y Q L * R S D * L I T V V A P K V K Q T
I N Y S G Q T K Y Y L * * L L S * K K P
I T V V K L R I I Y N S C C A K S K P N

19681 ATATTCTTAAACTAAAAATATTAAATACCTTGTGAAAATGATGCAATGTCTCAAATCTT 19740
* L F K S K * L K H F V K V V N C L K S
K Y S N Q N K Y N I S C K * * T V S N L
I L I K I K I I * P V S K S R * L T * F

19741 TTGCATTATATATTGAACCAATTACAACCAGTAATACTACCTGCATGTCCACTTAATGGA 19800
F T I Y L K T L T P * * S P R V P S N G
F R L I Y S P * H Q D N H H V Y L H I V
V Y Y I V Q N I N T M I I S T C T F * R

19801 ACACGATAATACTTACTGTTTCAACAACAATTCTAATTATTACATCTATGACAATAAAAA 19860
Q A I I F S L T T T L I L L T S V T I K
K H * * S H C L Q Q * S * Y H L Y Q * K
T S N H I V F N N N L N I I Y I S N N K

19861 TTTTATTATGTAGTAAAGGATGATTATATCGACAACCTTAACAAATGTTTTGCATCATAG 19920
L F L V D N G V L I A T S N N V F R L I
* F Y Y M M E * * Y L Q Q I T * L V Y Y
F I I C * K R S I Y S N F Q K C F T T D

19921 GCCGTGGTGGGACTTGAATTCTAAGAATCTTTAAACTTGTAACATAAACAACCTTCGTA 19980
R C W G S S L I R L F K F M S I Q Q F C
G A G G Q V * S E * F N S C Q Y K N S A
P V V R F K L N K S I Q V N I N T P L M

FIG. 3 CONT'D

19981 CAGGACACCCTAATACAATTCTATCAAACAAAACATCAAGGTGAATACCACRAACATTT 20040
 T R H S * T L S L K N Q L E V * P T Q L
 H G T P N H * L Y N T K Y N W K H H K Y
 D Q P I I N F I T Q K T T G S I T N T F

20041 ATGTGTCTAAACTTCAAGTAGCTTTTAAACTTATATGAAAACTACCAGCACTGTGACCG 20100
 Y V S K F N M S F K F I S K S P R S V P
 I C L N S T * R F N S Y V K Q H D H C Q
 V C I Q L E D F I Q I Y K K I T T V S A

20101 CGAAATCTTCGAAAATCTTTTCGTTCTTTACCACAAAAATAATCATGACTTTTTAATTCA 20160
 A K S A K L F A L F P T K I L V S F N L
 R K L L K * F L L F H H K * * Y Q F I L
 S * F S K S F C S I T N K N T S F F * T

20161 TCCAATAGTTACTAATTTCCAGGCGTTGCTCGACTAAATTTACCACACTAACACCTATTT 20220
 L N D I I L P G C R A S K F P T I T S L
 Y T I L S * L D A V L Q N L H H S Q P Y
 P * * H N F T R L S S I * I T H N H I F

20221 CAACCTCTTGAGTTTCAACTCAAAACCAAGCGATACTCTTTTCTACCACTGCTACAATAG 20280
 T P S S L T S N Q N A I L F S P S S T I
 L Q L V * L Q T K T R * S F L H H R H *
 N S F E F N L K P E S H S F I T V I N D

20281 AAGTCGGCTTGTCTGTGCGGATACGAGTTCGGTAATGACCTCGGGTGTTCATTAGATCCA 20340
 K L R V S L R H E L W * Q L G C P L R P
 R * G F L C G I S L G N S S G V L Y D L
 E A S C V A * A * A M V P A W L T I * T

20341 CCATTAACGCGCCCATACAGTAACCATTACTACGAGATTGTGCAAAATGATAGAAATGA 20400
 P L Q A P L T M P L S A R V R K V I K V
 H Y N R P Y H * Q Y H H E L V N * * R *
 T I A R T I D N T I I S * C T K S D K S

20401 GTCTCAGCACATAACAGTTCAAAACTTGGAGCGAGTCTAAATCTTGCCCTAAAATAACTA 20460
 * L R T N D L K S G R E S K S R S K I S
 E S D H I T L N Q V E S L N L V P N * Q
 L T T Y Q * T K F R A * I * F P I K N I

20461 TACCTACTATTAGACAAATAACGATTATACCAAATCTTCTGATACGTAACTAGTATAT 20520
 I S S L R N I A L Y P K S S * A N S * I
 Y P H Y D T * Q * I H N L L S H M Q D Y
 H I I I Q K N S F I T * F V I C K I M Y

FIG. 3 CONT'D

20521 CAAATACCATCAAATTTGGTATTTCAATATCCTCCAAACGTAAACGAATATCCGAATAAA 20580
T * P L K L W L T I P P K C K S I P K N
L K H Y N * G Y L * L L N A N A * L S I
N I T T K V M F N Y S T Q M Q K Y A * K

20581 GCATCCTTTTTTTTATAGATTAAACAATTAAGTTCTCAAAAATGTCATACTAAGATCATAA 20640
R L F F F D L K N I * S N K C Y S E L I
E Y S F F I * N T L E L T K V T H N * Y
T P F F F R I Q * N L L K * L I I R T N

20641 GTAAGTATAAAATAATGACTAGTCCTCACACCATCATCATTTCTCACAAACATGTCAATAA 20700
* E Y K I V S * S H P L L L L T Q V T I
E N M N * * Q D P T H Y Y Y S H K Y L *
M * I K N S I L L T T T T L T N T C N N

20701 CTAAATAATAATCTACTAAAACAAAGATAACAATTCAGTAATTTAAACTCAACACAATCA 20760
S K N N S S K T E I T L D N F K L Q T L
Q N I I L H N Q K * Q * T M L N S N H *
I * * * I I K N R N N L * * I Q T T N T

20761 TTTCAACAATTATAATTACAATAAAATTCCTAAAAGTTAAATACAACACCACATTACTA 20820
L T T L I L T S K L S K * N I N H H L S
Y L Q * Y * H Q N * P N E I * T T T Y H
F N N I N I N I K L I K L K H Q P T I I

20821 TTATTTTAATACTGAAAAATAGGATTTTACGTTCCGGTGATTACTAACCTTTGGACCGATA 20880
L L I I V K * G L I C A V L S Q F G P *
Y Y F * S K K D * F A L W * H N S V Q S
I F N H S K I R F H L G S I I P F R A I

20881 AGATACGGACAAAACATATTCATAAACTTACAAGGTAATCTCTCTCAGAGAAATACCTTA 20940
E I G T K Y L Y K F T G N S L T E K H F
N * A Q K T Y T N S H E M L S L R K I S
R H R N Q I L I Q I N W * L S D R * P I

20941 ATACCATTTGGATAATTAAACGGATGTCCGACATACTACTTACAACGATTCATGTGAGTT 21000
* P L G I L K G V P Q I I F T A L Y V *
N H Y V * * N A * L S Y S S H Q * T C E
I T F R N I Q R C A T H H I N S L V S L

21001 AATACAGTCATAAACTTATGATGTTGTAATCGACAAGGACAATTATACGCACAAAATGTA 21060
N H * Y K F V V V N A T G T L I R T K C
I I D T N S Y * L M L Q E Q * Y A H K V
* T L I Q I S C C * S N R N I H T N * M

FIG. 3 CONT'D

21061 AATCCACGTCCCAGACTATTTCTTCATCGAGGTCCAAGACGACAAAATTCTGTCAACCAAT 21120
K P A P D S L S T A G P E A T K L C H N
N L H L T Q Y L L L E L N Q Q K L V T T
* T C P R I P F Y S W T R S N * S L P *

21121 GGTAGACCATCATAAGAACATCTATTACTAAATTTGGGTAAACAATCGCTATCAAATCAA 21180
G D P L I R T S L S K F G N T L S L K T
V M Q Y Y E Q L Y H N L G M Q * R Y N L
W R T T N K Y I I I * V W K N A I T * N

21181 TGAATAAAACCTCTAACATACTGAAATGGTAAACTAACAGTAACCCCTAAACTATTATAGA 21240
V * K P S Q I V K G N S Q * Q S K I I D
* K N Q L N Y S K V M Q N D N P N S L I
S I K S I T H S * W K I T M P I Q Y Y R

21241 CTATACATACTAGGAGAATGATTTTATAACCACTAATATTACACTCATTCCTACCCAAA 21300
S I Y S G R V L F I P S * L T L L S P N
Q Y T H D E * * F Y Q H N Y H S Y P H T
I H I I R K S F I N T I I I H T L I P K

21301 AAATGAATGTAAACAGTAAATTAAGCACTATTTAATAGAAAACCCACCATCACATCGATAT 21360
K V * M Q * K I R S L N D K P P L T A I
K * K C K D N L E H Y I I K P H Y H L *
K S V N T M * N T I F * R Q T T T Y S Y

21361 TTTTAATGTCTCAAAAGAACCTTACGACTAAATATATTTAATTACTCAACAAAACGTAAA 21420
F I V S N E Q F A S K Y L N I L Q K A N
L F * L T K K S H Q N I Y I L S N N Q M
F N C L K R P I S I * I F * H T T K C K

21421 ACCTGTCAAAAAACATGATTACATTTACGAAGAAGATCACTTCCCAAAAATTATCCATAT 21480
Q V T K Q V L T F A E E L S P N K I P I
K S L K K Y * H L H K K * H L T K L L Y
P C N K T S I Y I S R R T F P K * Y T Y

21481 TTAATGGACCCATTTAGAAGAAAACCTTTATCTACCGTTACAATACGTACGATTGATAAAC 21540
F * R P L D E K S I S P L T I C A L * K
L N G P Y I K K Q F L H C H * A H * S N
I V Q T F R R K F Y I A I N H M S V I Q

21541 AAAACCTCTTTATCATGTTGTACCTTACGCCACGAATATCAAATAAACTATACTGATTT 21600
N Q L F L V V H F P P A * L K N S I V L
T K S F Y Y L M S H R H K Y N I Q Y S *
K P S I T C C P I A T S I T * K I H S F

FIG. 3 CONT'D

21601 AAAAGAACTTTAACCGACCGTGACGACAACAATTAATCTGGTCTAGTTAATTTACTA 21660
 N E K F N A P V A T T L K L G S * N F S
 I K K S I P Q C Q Q Q * N L V L D I L H
 K R Q F Q S A S S N N I * S W I L * I I

21661 AATCAAATAAGAGAATAAATTTCTCCATTTAATAATCAAGCGCTATGCGCATTCTCTAA 21720
 K T * E R I S L P L N N T R S V R L S I
 N L K N E * Q F L Y I I L E R Y A Y L S
 * N I R K N F S T F * * N A I R T F L N

21721 AAACAACCACTATCAGAACATTATGAACAATCTAGAGTAATTTAGATTGATACAATTA 21780
 K T P S L R T F V Q * I E N F R F * T L
 K Q Q H Y D Q L Y K N S R M L D L S H *
 K N T I T K Y I S T L D * * I * V I N I

21781 ATAAAAAATAAAAAATAAAGACAATACCAAAATTACTTGGAGAATTACAACACAGAGT 21840
 * K K I K K N R N H N * H V E * H Q T E
 N N K * K K I E T I T K I F R K I N H R
 I K K N K * K Q * P K L S G R L T T D *

21841 AAATTTGGTACTGACCAAAAATAAACCCTATCAGCAAGACTAACATTGGTATAATTATT 21900
 N L G H S T K I Q H Y D N Q N Y G Y * Y
 M * V M V P K * K T I T T R I T V M N I
 K F W S Q N K N P S L R E S Q L W I L L

21901 AAATTTTAAATTTTAAAACTAATAAACCTATAAGTGGGATCAAACACGTTGTTACCATT 21960
 N L F * F N Q N N P Y E G * N T C C H Y
 I * F N F I K I I Q I N V R T Q A V I T
 K F I L F K S * K S I * G L K H L L P L

21961 CTAAAGTAGATCACGGCCACTAAGATAAAAAATTCTCAAAAGTAAAGTGAGCTAAAATATT 22020
 S K M * H R H N * K * S N E N * E I K Y
 L N * R T G T I R N K L T K M E S S K I
 I E D L A P S E I K L L K * K V R N * L

22021 AATGTGACCGCTTCCACTAGTTTAATAAAAAATACTCCCACAATTAAAATTAGGAATAGT 22080
 N C Q R L H D F * K K H P H * N * D K D
 I V S A F T I L N N K I L T N I K I R I
 * V P S P S * I I K * S P T L K L G * *

22081 ATCTAAATTCACAAAAGGATTACCATCATTACTACATACCGAAGAATTGTTCCATTCTAA 22140
 Y I * T N E * H Y Y H H I A E * C P L I
 M S K L T K R I T T I I Y P K K V L Y S
 L N L H K G L P L L S T H S R L L T L N

FIG. 3 CONT'D

22141 AATAGCACGGAATATAAGATTATACCGGAAAAAAGCAATAGAAATGAAAACAACTATAAGG 22200
 K D H R I N * Y P R K E N D * K Q Q Y E
 K I T G * I R I H G K K T I K S K N I N
 * R A K Y E L I A K K R * R V K T S I G

22201 AATATTACAAAGAGAAAGATTCAAATTAAGAACATTTTCACTATAAAATAGTGAATTGTT 22260
 K Y H K E K * T * N K Y F H Y K I V * C
 R I I N R K R L K I R T F T I N * * K V
 * L T E R E L N L E Q L L S I K D S L L

22261 AGGATAAAAATAATTAATAAGATTCCCTCAAATAAAATGAAATAATCCAACAAGAGAAAT 22320
 D * K * * N N * P L K N * K I L N N E K
 I R N K N I I R L F N I K S * * T T R K
 G I K I L * E L S T * K V K N P Q E R *

22321 AAATCATGGCGAAACGGAAAAATTTAGATTGAAATCAGTCATGATAATATTGTATCTATG 22380
 N L V A K G K * I * S * D T S N Y C L Y
 I * Y R K A K K F R V K T L V I I V Y I
 K T G S Q R K L D L K L * Y * * L M S V

22381 ACCGAGACAAATACCAAAAAGATTACAACAAATAGGACTAAATCTGACATAAATATAAAG 22440
 Q S Q K H N K * H Q K D Q N L S Y K Y K
 S A R N I T K R I N N I R I * V T N I N
 P E T * P K E L T T * G S K S Q I * I E

22441 AGAATTTGGTCCAAGAATATTTCAAAGGTGGTGACGTGGAAAAAATAGGAATGGATGATT 22500
 E * V L N K Y L K W W Q V K K I R V * *
 R K F W T R I F N G G S C R K * G * R S
 R L G P E * L T E V V A G K K D K G V L

22501 TCGAGAGACAAAACATTTAGATTTGTTAAACATGGACATGTCCAACAACATAAGATCTAC 22560
 L E R N Q Y I * V I Q V Q V P Q Q N * I
 F S E T K I F R F L K Y R Y L N N I R S
 A R Q K S L D L C N T G T C T T S E L H

22561 CTTGTTGCTCGCACGGAGTCTATAAGAAATAGACAACGTACAGTTAACGGTATAACAAT 22620
 S C R A H R L Y K K I Q Q M D I A M N N
 P V V L T G * I N R * R N C T L Q W I T
 F L S R A E S I E K D T A H * N G Y Q *

22621 AAAAGCGTTAAGAAGACGATTAATACAACCGTTCATACTATAATTGGTGCCACTATCACC 22680
 N E C N K Q * N H Q C T H Y * G R H Y H
 I K A I R R S I I N A L I I N V V T I T
 K R L E E A L * T P L Y S I L W P S L P

FIG. 3 CONT'D

22681 AAAATAAGATAAAATAGACCAGAAAATATATTACAAAGAACATAAAGTATAATACCACA 22740
N * K * K I Q D K I Y H K K Y K M N H H
T K N R N * R T K * I I N R T N * I I T
K I E I K D P R K Y L T E Q I E Y * P T

22741 TAAAAATATACTATTAAAAATGTAGGTAACCGGGATAATAAGAAAACCATCCACAGGATG 22800
I K I H Y N * M W K A R N N K Q Y T D *
Y K * I I I K C G N P G I I R K T P T R
N K Y S L K V D M Q G * * E K P L H G V

22801 TAGAAGATAATAATTTGTAGGTTAAACACAAATACTAAAAAACGGATAATAAAATGTTCC 22860
M K * * * V D L K H K H N K A * * K V L
C R R N N F M W N T N I I K Q R N N * L
D E I I L C G I Q T * S K K G I I K C P

22861 ATAAAAATAATACAAATCGAAATGAAAAACAACAAAAGATAATAAAAACAATATATTGCT 22920
Y K I I N L K V K Q Q K E I I K T I Y R
T N * * T * S * K K N N K * * K Q * I V
I K N H K A K S K T T K R N N K N Y L S

22921 ATTTAGAGTAATTTAGATTTGTACAATAATTAATAAAAATAAAACGGATGTTGTAATCGA 22980
Y I E N F R F M N N I I K I K G V V N A
I F R M L D L C T I L * K * K A * L M L
L D * * I * V H * * N N K N Q R C C * S

22981 CAATATCCACTAAAATTAACATGATTAAACGATAATTACTAAATTTGTGGTGTCAAGGA 23040
T I P S K L Q V L K A I L S K F V V T G
Q * L H N * N Y * N Q * * H N L C W L E
N Y T I K I T S I K S N I I * V G C N R

23041 GCGTATTCACCTCATACAACACCTACAAAGAATACCAAACCCATGTATAATATATGAAC TA 23100
R M L S Y T T S T E * P K P V Y * I S S
E C L H T H Q P H K K H N P Y M N Y V Q
A Y T L I N H I N R I T Q T C I I Y K I

23101 GCACAAATAAATTTATGATGATATAATAAAATGACCAATAAAGGGATTTAGACCACGGTTA 23160
R T * K F V V I N N V P * K G L D P A L
D H K N L Y * * I I * Q N N G * I Q H W
T N I * I S S Y * K S T I E R F R T G I

23161 AAATCCCTAGATAGAAATTTTCCATGATGTATAAACTCATGAGAAACCATAGTCTTTGGG 23220
K L S R D K F P V V Y K L V R Q Y * F G
N * P D I K L L Y * M N S Y E K T D S V
K P I * R * F T S C I Q T S K P I L F G

FIG. 3 CONT'D

23221 AAAAATAGACTAAAATTATTACCATAAAAAAGATCTCAATTCTTATGATTCAACATACAA 23280
 K K D S K L L P I K E L T L F V L N Y T
 R K I Q N * Y H Y K K * L * S Y * T T H
 K * R I K I I T N K R S N L I S L Q I N

23281 TTATTTTGAAACATATCACTCAAATCATGATATCAATATCCATCACAAAAATAATTGTTG 23340
 L L V K Y L S N L V I T I P L T K I L L
 * Y F K T Y H T * Y * L * L Y H K * * C
 I F S Q I T L K T S Y N Y T T N K N V V

23341 AGAATATGATAACAACAAGTTGGAGTATTACCACAAAACCTCTAATGTGGAACAGTTATG 23400
 E * V I T T * G * L P T K S I V A Q * Y
 S K Y * Q Q E V E Y H H K P S * L K D I
 R I S N N N L R M I T N Q L N C S T L V

23401 TGATACACACTCATAGGAGTATGATAAACATTTAGATTTCATCAAGAGCATTACTTAGA 23460
 V I H S Y G * V I Q L D L P L E R L S D
 C * T H T D E Y * K Y I * L Y N E Y H I
 S H T L I R M S N T F R F T T R T I F R

23461 ACCGTAAAACTATTTAGACTTGGAACACAGACAAGTTCTTTTAAATGAATATTACAA 23520
 Q C K S L D S G K H R N L F F K V * L T
 K A N Q Y I Q V K T D T * S F N * K Y H
 P M K I F R F R Q T Q E L F I K S I I N

23521 AGATGTCTAACCAACATAAAAGTAAAAATAGTTCTTGACCGTGAAAAATACGAATAATA 23580
 E V S Q N Y K * K * * S R P V K * A * *
 K * L N T T N E N K D L V H C K K H K N
 R C I P Q I K M K I L F T A S K I S I I

23581 CGACTAAGACCGTACGGATGATGAAAAAATAAATCAAACATAGAACCATGAGAAAATAGA 23640
 A S E P M G V V K K N L K Y R P V R K D
 H Q N Q C A * * K K I * N T D Q Y E K I
 S I R A H R S S K * K T Q I K T S K * R

23641 GTAATAATACAAAACGGAAACTGAACATTACGATATAGAAGATTATGACTATTACTCTGA 23700
 * * * T K G K V Q L A I D E L V S L S V
 E N N H K A K S K Y H * I K * Y Q Y H S
 M I I N Q R Q S T I S Y R R I S I I L S

23701 AATGTTATAACCCAGTGTGGAAACAGATTTGCGGTTATAGAAGAATTTAACTGTTGGCA 23760
 K C Y Q T V G K D L R W Y R R L N S L R
 K V I N P * V K T * V G I D E * I Q C G
 * L I P D C R Q R F A L I K K F K V V T

FIG. 3 CONT'D

23761 CCACAATAATGATTACGACAACAAAGATCATCAAAGAAATCGCTCTAAGTTACATTT 23820
P T I V L A T S Q E L L K K L S I * H L
H H * * * H Q Q N N * Y N R * R S E I Y
T N N S I S N I T R T T E K A L N L T F

23821 TGATTTAGAAATAATGGATTATGACCACAAATACTGAATAGACCAAAATGACAATTCGGA 23880
V L D K N G L V P T * S K D P K V T L G
F * I K I V * Y Q H K H S I Q N * Q * A
S F R * * R I S T N I V * R T K S N L R

23881 CAACGTTGACATGTAGCAGCATAAGGACTAAATGGACTAACACTGTAACATTTACCGAA 23940
T A V T C R R I G S K G S Q S M S L H S
Q Q L Q V D D Y E Q N V Q N H C Q Y I A
N C S Y M T T N R I * R I T V N I F P K

23941 TTGTTAAAATTACATGGGAGTGGAGAATTAACCCCTTGCATTTTAAAAAAGATTAACGTTG 24000
L L K L T G E G R L Q S R L I K E L Q L
* C N * H V R V E * N P V Y F K K * N C
V I K I Y G * R K I P F T F N K R I A V

24001 AAATTAACTCATGAAACGAAGCAAATCAAGTATGACTAAGAAAAAGAACATTATTAAAA 24060
K L K L V K S R K T * V S E K E Q L L K
S * N S Y K A E N L E Y Q N K K K Y Y N
K I Q T S Q K T * N M S I R K R T I I K

24061 CTACTTAGATTCTATATACCATCAACAAAATTCATACAAAATCTATTTAAACGGTAT 24120
S S D L I Y P L Q K L L I T K S L N A M
Q H I * S I H Y N N * S Y Q K L Y I Q W
I F R L Y I T T T K L T N N * I F K G Y

24121 GGGTTGAGGTCTGCTAGACTAAACGTCAACCCGTCAAGACCAAAAGACGTTAGAAGATTA 24180
G L E L R D S K C N P L E P K R C D E L
V W S W V I Q N A T P C N Q N E A I K *
G V G S S R I Q L Q A T R T K Q L R R I

24181 ATATTTTAACTGTGATGAAGATCAAGAACAGTTAACATAATATCAAACGGACGTTAATTA 24240
* L I S V V E L E Q * N Y * L K G A I L
N Y F Q C * K * N K D I T N Y N A Q L *
I F N V S S R T R T L Q I I T Q R C N I

24241 CAATGATAATTATTAATATTAGGAAGAAGAACCTTATCTTCATACCAAAATTATTAAAA 24300
T V I L L * L G E E Q F L L Y P K L L K
H * * * Y N Y D K K K S Y F T H N * Y N
N S N I I I I R R R P I S P I T K I I K

FIG. 3 CONT'D

24301 TTAAACTCGAGAGTATCACAACAAATGAGTGCAATAACAAAAAGACAATTATTATGAAAA 24360
L K L E * L T T * E R * Q K E T L L V K
* N S S E Y H Q K S V N N N K Q * Y Y K
I Q A R M T N N V * T I T K R N I I S K

24361 ACAGGAACACGATTGGAAGAAAACGAAGTTCAACGTTCTCAGTATTTGGTGAAGACGA 24420
Q G Q A L G E K A E L Q L L * L G G E A
K D K H * V K K Q K L N C S D Y V V K Q
T R T S F R R K S * T A L T M F W R R S

24421 AGGACAGGATAACCATGATTAATAGCAAGAACACTCTCATGATGACATGAGCTGGTGTGA 24480
E Q G I P V L * R E Q S L V V T S S W V
K R D * Q Y * N D N K H S Y * Q V R G C
G T R N T S I I T R T L T S S Y E V V S

24481 CTGACCACATCCACAAGAACAATGGACTAGGATATTGACGAATACTGGGATCCAGAACA 24540
S Q H L H E Q K G S G I V A * S G L D Q
Q S T Y T N K N V Q D * L Q K H G * T K
V P T P T R T * R I R Y S S I V R P R T

24541 AGAGTTTTTTTCAGAGACCAACCACAACCCTTGTAACACGTCCCAAGCCACAACACTACTT 24600
E * F F D R T P T P S C Q A P N P T S S
N E F F T E P Q H Q H V N H L T R H Q H
R L F L R Q N T N T F M T C P E T N I F

24601 CTTTTACACCACATAACCTACCTAGTATATTACAAAGAACAGAAACATCATGACTACGG 24660
S F H P T N S P D Y L T E Q R Q L V S A
L F T H H I P H I M Y H K K D K Y Y Q H
F L T T Y Q I S * I I N R T K T T S I G

24661 AAAGATCCAACCAGAATACTGTGAACGCAGTCATTGTTGGCAACATTATAAAAAAGATTA 24720
K R P Q D * S V Q T L L L R Q L I K E L
R E L N T K H C K R * Y C G N Y Y K K *
K * T P R I V S A D T V V T T I N K R I

24721 AAATAAAATTTACCATAGTTATCACCATGGTGAACAAGATTACTAAATAACGTCGGATTA 24780
K I K F P I L L P V V Q E L S K N C G L
N * K L H Y * Y H Y W K N * H N I A A *
K N * I T D I T T G S T R I I * Q L R I

24781 TGACTTCAAAAATGACTACAAACACAACCTAATGCTGGAAATACCATAATGTCCTGTTCCA 24840
V S T K V S T Q T S * S R * P I V P C P
Y Q L K * Q H K H Q N R G K H Y * L V L
S F N K S I N T N I V V K I T N C S L T

FIG. 3 CONT'D

24841 TAAAAATTTCTTCAAAGACGACAAATAATATTATCAACCGTTTGTAGAAAACATACTAAGA 24900
I K L S T E A T * * L L Q C F R K Y S E
Y K * L L K Q Q K N Y Y N A F D K T H N
N K F F N R S N I I I T P L I K Q I I R

24901 TTACCGTTGTAATAACCAAAATTTCTAAAACAATGATTATTTGTATATTATAAAAGGGA 24960
L P L M I P K L S K T V L L V Y L I K G
* H C C * Q N * L N Q * * Y F M Y Y K G
I A V N N T K F I K N S I F C I I N E R

24961 ACAATACGTCCTTCTCAAAGACGACGAAAAGTAGTTTACGAAGGAGAAACCGAAATGAA 25020
Q * A P L T E A A K * * F A E E K A K S
K N H L F L K Q Q K E D F H K R K P K V
T I C S S N R S S K M L I S G R Q S * K

25021 ATAGCATTAAATTTTACATCGATACAAAACCTTATTATAAAGAAATTGATGAGTCGGTATA 25080
* R L K F H L * T K F L I E K V V * G Y
K D Y N L I Y S H K S Y Y K K L * E A M
I T I * F T A I N Q I I N R * S S L W I

25081 AAACATCAATAGAACCAACGCAAAAATTACGACTATTAAATTGACTAATAAGACAAAGA 25140
K S L * R P Q T K L A S L K V S * E T E
N Q Y N D Q N R K * H Q Y N L Q N N Q K
K I T I K T A N K I S I I * S I I R N R

25141 AGAACACGAGAAGCGTACCCATCACCAAAAACACAATAATTTGAGTGGAAGAAGAAGG 25200
E Q A R R M P L P K Q T S * L E G E E E
K K H E E C P Y H N K H Q N Y S V K K K
R T S K A H T T T K T N I I V * R R R G

25201 AGAAGCGCAGCATTTGCATCTTCATAAAGACGAAGAATAGCAAAACAATGAAAACCTTGGG 25260
E E R R L R L L I E A E * R K T V K S G
R K A D Y V Y F Y K Q K K D N Q * K Q V
R R T T F T S T N R S R I T K N S K F G

25261 AAATTACAGTCAAAACAATTACTGTCTATAACTCAGACACCCACCAGAAATACTCTAGTTT 25320
K L T L K T L S L I S D T P P R * S I L
R * H * N Q * H C Y Q T Q P H D K H S *
K I D T K N I V T N L R H T T K I L D F

25321 TAAGGGTGATTGAAATGATATCAACCAGTTCTCCTTAAATAAGTTTGATTAGAGGATTT 25380
I G V L K V I T P * S S N I * V L E G L
F E W * S * * L Q D L P I * E F * N E *
N G S V K S Y N T L L F K N L S I R R F

FIG. 3 CONT'D

25381 CAATGATAACTAACAAGAAATAAACAGACAAGATTAATACGTCGAACGGTACTGAATAAC 25440
T V I S Q E K N T Q E L * A A Q W S K N
L * * Q N N K I Q R N * N H L K G H S I
N S N I T R * K D T R I I C S A M V * Q

25441 AGTCTCATACCGTGAAAAACACTATTATAATTATCATAAAATCTACTTCAATTACCAAAT 25500
D S Y P V K Q S L I L L I K S S T L P K
T L T H C K K H Y Y * Y Y K L H L * H N
* L I A S K T I I N I T N * I F N I T *

25501 GAACTATGATGAGTTAACGTACATCGACTATGAGAATACGTTCCACAGTGTGAATCGAGG 25560
S S V V * N C T A S V R I C P T V S L E
V Q Y * E I A H L Q Y E * A L H * V * S
K I S S L Q M Y S I S K H L T D C K A G

25561 TTAGAATTATGATTAAACGTAAACTACAACACTATTATAATTAAATTTAGGGATCAACCT 25620
L R L V L K C K S T S L I L K L D R T P
W D * Y * N A N Q H Q Y Y * N * I G L Q
I K I S I Q M K I N I I N I K F G * N S

25621 ACAAATCCAGGTGTGACGCCAAGAAGAAGAGCAAGAAAAAACTTCTAAATAACAACTG 25680
H K P G C Q P E E E R E K K S S K N N S
I N L D V S R N K K E N K K Q L N I T Q
T * T W V A T R R R T R K K F I * Q K V

25681 TTTCAATTTGAAAGTCTACAACCAAAACAACTTCTGAATATTGTTAACATGACCACCATCA 25740
L T L S E S T P K T S A * L L Q V P P L
C L * V K L H Q N Q Q L K Y C N Y Q H Y
F N F K * I N T K N F S I V I T S T T T

25741 CTTAATCTCTAGAAGAAACACATGTTAGGAAATTACCATAATTTCAAAACGGAGGATAA 25800
S I L S R R Q T C D K L P I L T K G G I
H F * L D E K H V I R * H Y * L K A E *
F N S I K K T Y L G K I T N F N Q R R N

25801 AACAGACTTAGAGTTTAAAGACCAATGTGGTGTGGCGATGACAACGACGATACAAAGGT 25860
K D S D * I E P * V V A A V T A A I N G
K T Q I E F K Q N C W L R * Q Q Q * T E
Q R F R L N R T V G C G S S N S S H K W

25861 GGTACCAGTCGTCGTCGACCGTATGGTAAAAGAGAATTACATGTTATATCTTAATTACCA 25920
G H D A A A P M G N E R L T C Y L I L P
V M T L L L Q C V M K E * H V I Y F * H
W P * C C S A Y W K R K I Y L I S N I T

FIG. 3 CONT'D

25921 AACCCACAATGATACCTACAAGAATTATTTTTAGTTTTCAACTATCGATGACGAAAATTA 25980
K P T V I S T R L L F * F N I A V A K L
N P H * * P H E * Y F D F T S L * Q K *
Q T N S H I N K I F I L L Q Y S S S K I

25981 TTACGAGAAGAAAGATAAGTCTTACCAAAATCACGATGGTTGAGACGTGAACGATTTTAT 26040
L A R R E I * F P K L A V L E A S A L I
Y H E E K * E S H N * H * W S Q V Q * F
I S K K R N L I T K T S G V R C K S F Y

26041 GTTTCACAACAATTAAGATTACGAGTTCGTGAATTATCAAACAATGTCGTTAATAAATTA 26100
C L T T L E L A * A S L L K N C C N N L
V F H Q * N * H E L V * Y N T V A I I *
L T N N I R I S L C K I T Q * L L * K I

26101 TTTAACCACGTTAATCAAGAAGAAATGTTCTTTAAATAGAGCAGAGCTACGAAATCTC 26160
L N P A I L E E K C S I K D R R S A K S
Y I Q H L * N K K V L F K I E D R H K L
F K T C N T R R * L F N * R T E I S * L

26161 CGAGTCCAAGTCTAACTATCCGAATAATTACCAGCAAATTGACGAAATTTACGAATACAG 26220
A * T * I S L S I L P R K V A K F A * T
P E P E S Q Y A * * H D N L Q K L H K H
S L N L N I P K N I T T * S S * I S I D

26221 AGAGTTGTCGAATCACTATAAAGAGAACATTTTAAACCACGACGAAATCGATACCTCTTC 26280
E * C S L S I E R T F N P A A K A I S F
R E V A * H Y K E Q L I Q H Q K L * P S
R L L K T I N R K Y F K T S S * S H L L

26281 CAATTACTCACACAATTTTCAGTTAGAGGAGCATAATTA AAAACACCATTACCATAGTA 26340
T L S H T L L * D G R I L K Q P L P L *
P * H T H * F D I E E Y * N K H Y H Y D
N I L T N F T L R R T N I K T T I T I M

26341 TAAACAGTAATCAAGTTTTACGAGGAATACCAACAACAAATACGTAAATCAATATTT 26400
I K D N T * F A G * P K N N I C K L * L
Y K T M L E F H E K H N T T * A N * N Y
N Q * * N L I S R I T Q Q K H M K T I F

26401 GGATAAAGAAAATTTTGACAAAATCATTGACGACCAACACATATAGTCCACTACATCCA 26460
G I E K L V T K T L G P K H I D P S T P
V * K K * F Q K L L D Q N T Y I L H H L
R N R K F S N * Y T R T Q T Y * T I Y T

FIG. 3 CONT'D

26461 TAACGTGGATTGTGCCATAAAATAATTTGTATTACTAGTAACCTACAAGTGACCATCA 26520
I A G L C P Y K I L C L S * Q I N V P L
Y Q V * V L T N * * V Y H D N S T * Q Y
N C R F L P I K N F M I I M P H E S T T

26521 AGAATGATAATAGGACTTGGTTAAAGTCTATTTTTACAACAAAATACTTATGAACAAGA 26580
E * * * G S G I E S L F T T K I F V Q E
N K S N D Q V L K L Y F H Q K * S Y K N
R V I I R F W N * I F I N N K H I S T R

26581 CAATTAAGTATTTTCGCGGAGAACAAATAAACTTAGTAAGACATGGTTTAAACAGACTA 26640
T L K V L A G R T * K F * E T G F N D S
Q * N * * L A E Q K N S D N Q V L I T Q
N I K S F R R K N I Q I M R Y W F Q R I

26641 AAACCTAGACTCAATAGAGTAACCAAATTTTAGTTGTAGGTAACGCGGATTAACTGA 26700
K S D S N D * Q N L F * V D M A G L K V
N Q I Q T I E N T * F D F M W Q A * N S
K F R L * R M P K F I L C G N R R I Q S

26701 AATTTAGAAGTATGATAATTACGATGAAAAAATCTAAACATAATACTCTACTTAGAATAA 26760
K F R * V I L A V K K S K Y * S I F R I
K L D E Y * * H * K K L N T N H S S D *
* I K M S N I S S K * I Q I I L H I K N

26761 GTTCTCAGATAATTCAGAAACTTATTATCAATATAGTTAGAATTTCTATATCCATGTATA 26820
* S D I L D K F L L * I L R L S I P V Y
E L T * * T K S Y Y N Y * D * L Y L Y M
L L R N L R Q I I T I D I K F I Y T C I

26821 CTTTACATACATTTTACCGGAACCATACAAACCGATGATTAAAGAAAAAGTAAATATTAT 26880
S I Y T F H G Q Y T Q S S I E K E N I I
H F T H L I A K T H K A V L K K K M * L
F H I Y F P R P I N P * * N R K * K Y Y

26881 AAGGAACATAACGAGAAAAAATATACAACAACATGACCAACACCAAGACGTACAAAATCA 26940
N R T N S K K I H Q Q V P Q P E A H K L
I G Q I A R K * I N N Y Q N H N Q M N *
E K Y Q E K K Y T T T S T T T R C T K T

26941 TTTACAGTATTAACAACACTACTCATACCACCTAGTACTAAAACAATAGTTTGTAGA 27000
L H * L Q Q S S Y P P * * S K T I L V D
Y I D Y N N H H T H H D D H N Q * * F M
F T M I T T I L I T T M M I K N D F C R

FIG. 3 CONT'D

27001 GTACTACTAATCTTAGAGAACAGTCTAGAGTAATTTAGATTGAAATAAATACCTGCAAA 27060
 * S S * F R K D S R M L D L S * K H V N
 E H H N S D R T L D * * I * V K N I S T
 M I I L I E Q * I E N F R F K I * P R K

27061 CCTCTGGATCGATGTGTGTAAGAGAACAAATAATCTCTTAAACCACAATGTTTGGAACCTC 27120
 P S R A V C M R K N N S F K T N C V K F
 Q L G L * V C E R T I L S N P T V F R S
 S V * S C V N E Q * * L I Q H * L G Q L

27121 TAAACACAGATTTTCATATTAATGACAGTTGGATAACAACCAATGACATAACATGGAAATT 27180
 I Q T * L I I V T L R N N T V T N Y R *
 S K H R F Y L * Q * G I T P * Q I T G K
 N T D L T Y N S D V * Q Q N S Y Q V K L

27181 TACAAACCACAGCGTTCAAACCGTTTAAACGAAGAGTGAAATGTAATGCATCAGTGCTAT 27240
 I N P T A L K A F K S R V K C * T T V I
 F T Q H R L N P L N A E * K V N R L * S
 H K T D C T Q C I Q K E S * M V Y D R Y

27241 AAAGGGTATCATTATTAAAAACCACAACATTGATCAAAATGATGAATACCATTATGACAAA 27300
 N G M T I I K T N Y S T K S S I T I S N
 I E W L L L K P T T V L K V V * P L V T
 K G Y Y Y N Q H Q L * N * * K H Y Y Q K

27301 GACTCCGACACAGATCTAATCAACTTAGTCTGAAGACTTAAATAACAAACCGCACGCTCC 27360
 R L S H R S * N F * S R F K N N P T C L
 E S A T D L N T S D A E S N I T Q R A S
 Q P Q T * I L Q I L K Q I * Q K A H L P

27361 GTGAATTATTCATACCAACTAAATAAAAAAGTTACTATGACGAACCATGTATCCTGTCTAA 27420
 C K I L I T S K N K L S V A Q Y M P C I
 A S L L Y P Q N I K * H Y Q K T C L V S
 V * Y T H N I * K E I I S S P V Y S L N

27421 AATCAAAATCAAAATAAAACAGAATAAAGAAATTAGAAACAACAACGAAAAAATCGTTGA 27480
 K T K T K N Q R I E K I K T T A K K A V
 K L K L K I K D * K K L R Q Q Q K K L L
 * N * N * K T K N R * D K N N S K * C S

27481 TAATTCGAAACATACGTTGAAACACCAAAAACATTAAAGAAATAATAAAGTGGAAGCCGA 27540
 I L S Q I C S Q P K Q L K K I I E G E A
 * * A K Y A V K H N K Y N R * * K V K P
 N L K T H L K T T K T I E K N N * R R S

FIG. 3 CONT'D

27541 ATGCAATATTTTCTCCATACGTCAACATATTCAGAATATCACTTGTTCATATGGTGGG 27600
 * T * L L P I C N Y L D * L S C T I G G
 K R K Y F L Y A T T Y T K Y H V L * V V
 V N I F S T H L Q I L R I T F L N Y W G

27601 TGAAGTCTAATAAATTAGATTTAGATTTGTAATACTTATTTAGAAAAGAAGGAGTTAAAT 27660
 V E S * K I * I * V N H I F R K K R L K
 W K L N N L R P R F M I F L D K R G * N
 S * I I * D L D L C * S Y I K E E E I *

27661 GAAGACTAGTTCGACAATGTAAGAATTTTCTTACCTTAAAGAGAAACCCACATTATGATG 27720
 S R I L S N C E * F F P I E R Q T Y Y *
 V E S * A T V N K F S H F K E K P T I S
 K Q D L Q * M R L L I S N R K P H L V V

27721 AAAAATAATGATAGTATAACGTCAAGCCAATATGCTCGGCATCATACAAACAAATAGAAT 27780
 K K N S D Y Q L E T I R A T T H K N I K
 S K I V I M N C N P * V L R L I N T * R
 K * * * I A T R N Y S G Y Y T Q K D *

27781 AGTTCTACTAATAAGAAACCGAATACACCGGTAAGTATAGTGGAACTGATATAAATTAA 27840
 D L H N N K P K H P W Q S D G Q S Y K I
 I L I I I R Q S I H G N V I V K V I N L
 * S S * E K A * T A M S * * R S * I * N

27841 CAAAAATACGAAACTTATTACGAAAAGAACGTAAAAGATATCACAAATGATAATAAAGAT 27900
 T K I S Q I I S K K C K R Y H K S N N R
 Q K * A K F L A K R A N E I T N V I I E
 N K H K S Y H K E Q M K * L T * * * K *

27901 AACAAATATACCTAAGAAATAAAACAATTATCATAAGCCGAAAATAATCTTGACCGTCAA 27960
 N N Y P N K I K N I T N P K K N S S A T
 I T I H I R * K T L L I R S K I L V P L
 Q * I S E K N Q * Y Y E A K * * F Q C N

27961 CCACCTCAAAATTAGGTCTCTGGTTATTAGAATACACATAACTATACTTTCCGTTCTACA 28020
 P P T K I W L G I I K H T N I H F A L H
 Q H L K L G S V L L R I H I S I F P L I
 T S N * D L S W Y D * T Y Q Y S L C S T

28021 AACAAATCCGGTCAATAACTCCTGATAGTGTGTAATTGACGATGACAATAAGCACCAGTAG 28080
 K N P W N N L V I V C * S S S N N T T M
 N T L G T I S S * * V N V A V T I R P *
 Q * A L * Q P S D C M L Q * Q * E H D D

FIG. 3 CONT'D

28081 AAATATATGTCCACAGTTTGAACCGTGACCAATATGAGAAAGTCTAAACGGGCATATAC 28140
K I Y L T D F K A S T I S K * I Q G Y I
R * I C P T L S P V P * V R E S K G T Y
K Y V P H * V Q C Q N Y E K L N A R I H

28141 AATGACATCGATTCCACGTTTCATGAAACATGGATATTTGCACGGAAAAATCTATTCAATC 28200
N S Y S L H L Y K T G I F T G K * I L *
T V T A L T C T S Q V * L R A K K S L N
* Q L * P A L V K Y R Y V H R K L Y T L

28201 TACAATTATCACCAAAACGACAAAAACAATTGAGATTTCACCATTTGATAGCAAATGGCA 28260
I N I T T K S N K N L R F N T V I T * R
S T L L P K A T K T L D L T P L * R K G
H * Y H N Q Q K Q * T * L Q Y S D N V T

28261 GATCATTGGATCACCATACCTATGACGGAACAATTCTCGAATTTAGATTTGATAATCCT 28320
R T F R T T H I S G Q * S S L D L S N P
D L L G L P I S V A K N L A * I * V I L
* Y V * H Y P Y Q R T L L K F R F * * S

28321 ACAGAATATGAGGGCCAGTAATACGACCTTCATCTCGAGGAGACCTTTAGCAAGTCCTT 28380
H R I S G T M I S S T S A G R S I T * S
I D * V G P * * A P L L L E E P F R E P
T K Y E R D N H Q F Y F S R Q F D N L F

28381 AGGAGTCTTTTGAAGAACCCGACTGGTTAGACTCGCTTTAATGGTTTGGAAATTATCTC 28440
D E L F S R P S V L R L S I V L G K I S
I R L F V E Q A S W D S R F * W V K L L
G * S F K K P Q G I Q A F N G F R * Y L

28441 CGTCTTTTGGGTTGGATTTAAGTGACACAGATGACTTGGTGTTCCCTTTATGATAGGGTG 28500
A S F G L R F E S H R S L W L S I S D W
P L F V W G L N V T D V * G C P F V I G
C F F G V * I * Q T * E V V L F Y * G V

28501 TAATAAGGACCAAGAGGCCCTAGTGAGTTAAAGTTTTCATCTCTGAAATTTAAAAGTC 28560
M I G P E G P D S L K L F T S V K F K *
C * E Q N E P I V * N * F P L S K L N E
N N R T R R S * E I E F L Y L S * I K L

28561 TACCAGTTCCTCAAGGGTAACGAAAGCCTCATGGGGGAAGACTTCGTTTTCTATAACCA 28620
I T L S N G N S E S Y G R R F C F S I P
S P * P T G M A K P T G G E S A F P Y Q
H D L L E W Q K R L V G K Q L L L I N T

FIG. 3 CONT'D

28621 TATCTGTGTCCGCCGCAAGAAAATTTTGTGCGACTACCGATTGTTTTCGTCAACAATGGCT 28680
I S V A P T R K F C S I T L L L L Q * R
Y L C L R R E K L V A S P * C F C N N G
Y V C G A N K * F L Q H D V F A T T V S
, .

28681 CTACCATAAAGATGATAGAGCCATGGCCGGGTATACGGTTACGTAGGATACCACTTAGGG 28740
S P I E V I E T G A W I G I C G I T F G
L H Y K * * R P V P G Y A L A D * P S D
I T N R S D R Y R G M H W H M R H H I G

28741 AGCTTCCCCAGAAGACCCCAACGATTAGTGGTTCGACTGTGAAGATGAGGGAGGCTACAAA 28800
E F P D E P N S I V L S V S R S G G I N
R S P T K Q T A L * W A S V E V G E S T
R L P R R P Q * D G L Q C K * E R R H K

28801 GCAGTTCCTTAGGATGATGAGTTCCTCGATAGGGATGATCCAAAGCGGACCATGCTAAA 28860
R * P I R S S L F S D R S P K R R T R N
E D L S G V V * S A I G V L N G G P V I
T L P D * * E L L * G * * T E A Q Y S K

28861 ACGGAGTTCGATAATAACAACCTCCGAGTCCTCCAGACGAAGATTATCAGCTGGTCCAA 28920
Q R L A I I N F A * S P R S R I T S W T
K G * P * * T S P E P L D A E L L R G P
A E L S N H Q L S L F T Q K * Y D V L N

28921 GTGCAAGAGTTAGTGCACCTGGGTATTAGCAAGTAATTCATCTTCATTAGATTAAAAAT 28980
* T R L * T S G I I T * * T S T I R I K
E R E * D R P G L L R E N L L L L E L K
V N E I V H V W Y D N M L Y F Y N * N *

28981 CTGTAAGTCTAAGATATCATTTTGGACTATACCGACTACTCTAGCGATTAGAACAAAATC 29040
S M * I R Y Y F R I H S I L D S I K N *
L C E S E I T F G S I A S S I A L R T K
V N L N * L L V Q Y P Q H S R * D Q K L

29041 GGTTCGAACCATTTCTAAGATTTGGAGTCGTTTCAGTGATTGTTTTACGGTTCCTTTAGT 29100
G L K T F I R F R L L D S L L I G L F D
A L S P L S E L G * C T V L C F A L S I
W A Q Y L N * V E A L * * A F H W P P *

29101 CCGTATTTTAAATTTGTTTTGGAGCGGTTTTCGCTTGAGGATTATTTGTAACATTACAAG 29160
P M F N * C F R A L L S S R I F M T I N
L C L I K V F G R W F R V G L L C Q L T
A Y F K L L V E G F A F E * Y V N Y H E

FIG. 3 CONT'D

29161 TTGTCACAAAACCATTTTCTCCTGGAAGAGTTTTAAACCATTACGACTTTACAATTCG 29220
 L L T K T F S S R R L I K T I S F H * L
 * C H K P L L P G E * F K P L A S I N F
 V T N Q Y F L V K E F N Q Y H Q F T L A

29221 AACCATGATTACTAGGAGTCAAAGGATAAGAACGTCTTAATCGAGGATGTGGTCCACGAA 29280
 K T S I I R L K R N K C F * S R C W T S
 S P V L S G * N G I R A S N A G V G P A
 Q Y * H D E T E * E Q L I L E * V L H K

29281 AAAAGAAACCAAGATTTAATCTGAACCAATTTTCTCTAAGGCTCCGACTGAGTGGACAAT 29340
 K E K T R F * V Q N F S I G L S V * R N
 K K K P E L N S K T L L S E S A S E G T
 K R Q N * I L S P * F L N R P Q S V Q *

29341 TTCTACAAAACTTGAAGTAATAAGACCAAGATAATCCAACTATCATGAAATGGTCCGA 29400
 F I N K F K M I R T R N P K I T S * W A
 L S T K S S * * E P E I L N S L V K G P
 L H K Q V E N N Q N * * T Q Y Y K V L S

29401 AACTCTGTTAATACTTTCAAGAACTTCTCTTAAATTTACGAATGCAATTAAGATTAGTCT 29460
 K L C N H F N K F L I * I S V N I R I L
 K S V I I F T R S S F K F A * T L E L *
 Q S L * S L E Q L S N L H K R * N * D S

29461 TGTGACTAAGACTAAGCAACTCAAGATTTGGAGTCGCATTTTCTCCACAATTTGTTAATG 29520
 V S I R I R Q T R F R L T F S T N F L *
 F V S E S E N L E L G * R L L P T L C N
 C Q N Q N T S N * V E A Y F L H * V I V

29521 GTCTTGTCAAACTGAGAGAATTAAATTCACGACCATGAGTCGTGTAAAGTTTACTAAAAT 29580
 W F L K V R K I * T S T S L V N * I I K
 G S C N S E R L K L A P V * C M E F S K
 L V T Q S E * N L H Q Y E A C K L H N *

29581 GAGGACTCCTAGTATCAAATGAACGATGAGAACTACTAGGAATACATCTTCTGAGACAAC 29640
 S R L I M T * K S S K I I R I Y F V R N
 V G S S * L K S A V R S S G * T S S E T
 E Q P D Y N V Q * E Q H D K H L L S Q Q

29641 GAATTACTCTTACTTAGGATTAAGCTGTGATCCACCATTGGGGAGCGATAATAAGCCTTA 29700
 S L S F S D * N S V L H Y G R A I I R F
 A * H S H I R I R C * T T V G R * * E S
 K I L I F G L E V S P P L G E S N N P I

FIG. 3 CONT'D

29701 TCCTGTGAGAGATAGTCTTACTTAAGAACGACATTATTGTCTATCTCATCCAACAATGTC 29760
L V S E I L I F E Q Q L L L Y L L N N C
Y S V R * * F S N K S Y Y C I S Y T T V
P C E R D S H I R A T I V S L T P Q * L

29761 TGATATATAATTAATCATCTTTAAATATAAATCTGTAAACTAACAATCTCATCAATATT 29820
V I Y * N T S I K Y K S M Q N N S Y N Y
S * I N I L L F K I N L C K I T L T T I
S Y I L * Y F N * I * V N S Q * L L * L

29821 CCAAATCGACATCATATTTGCGGAGGCCCTTCTCGATAGTTAACATCACAAATTATATAT 29880
P K A T T Y V G G P L A I L Q L T * Y I
L N L Q L I F A E P F L * * N Y H K I Y
T * S Y Y L R R R S S S D I T T N L I Y

29881 ATAATCATATACTAACTTTAATTAATATCGGAAAACCTCCTTAATGTTTTTTTTTTTTTTT 29940
Y * Y I I S I L * L R K S S N C F F F F
I N T Y S Q F * N Y G K P P I V F F F F
I L I H N F N I I A K Q L F * L F F F F

29941 TT 29942
F
F

FIG. 3 CONT'D

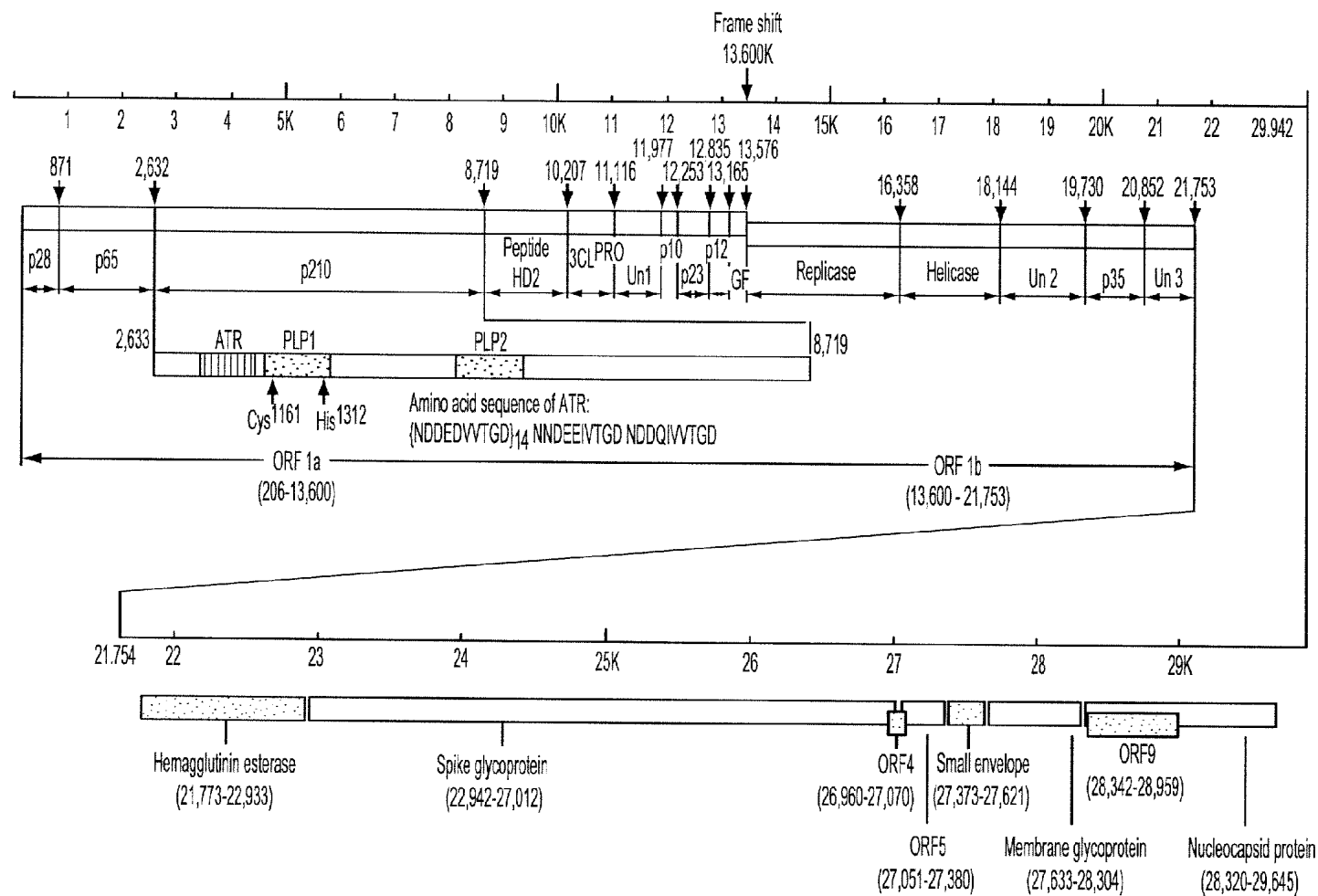


FIG. 4

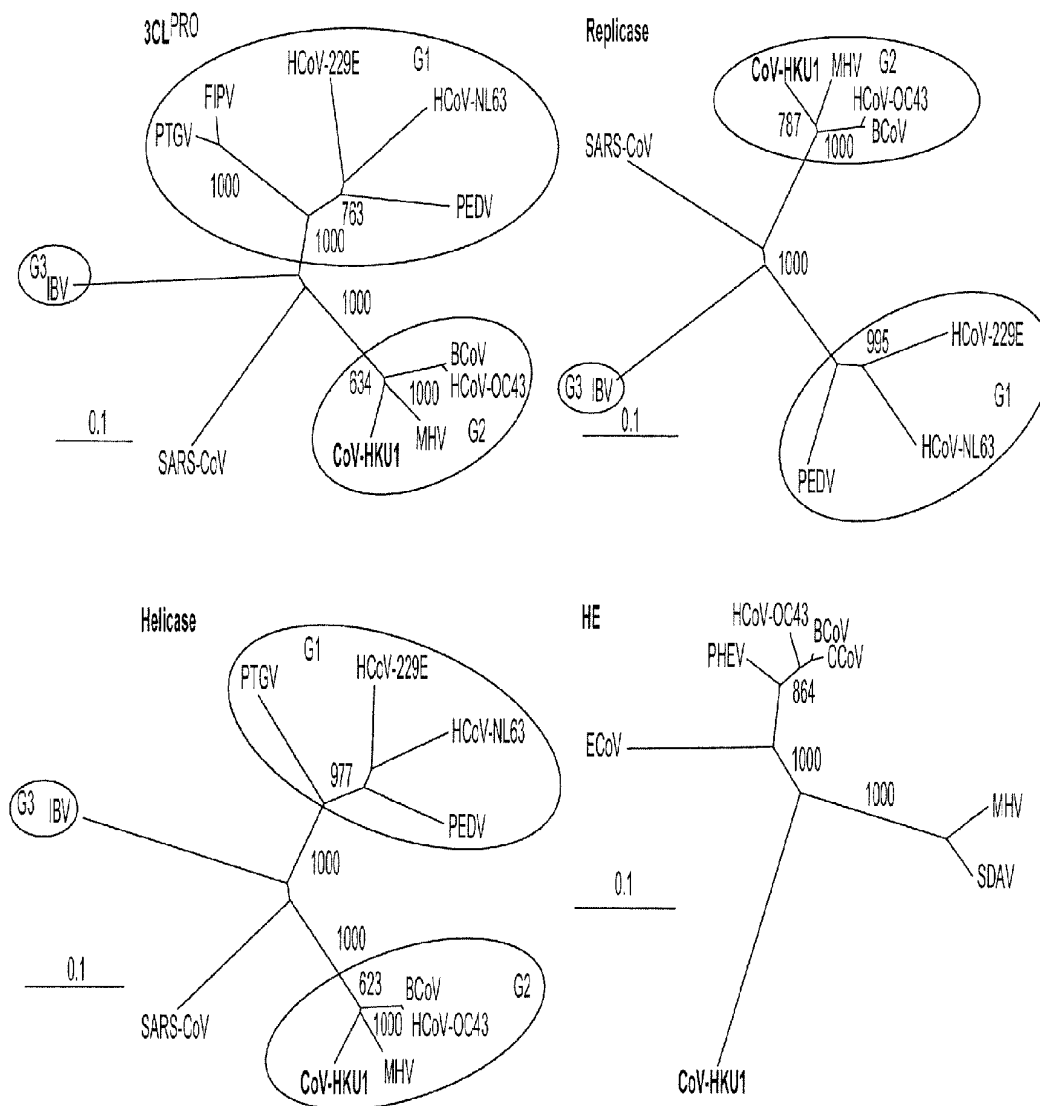


FIG. 5A

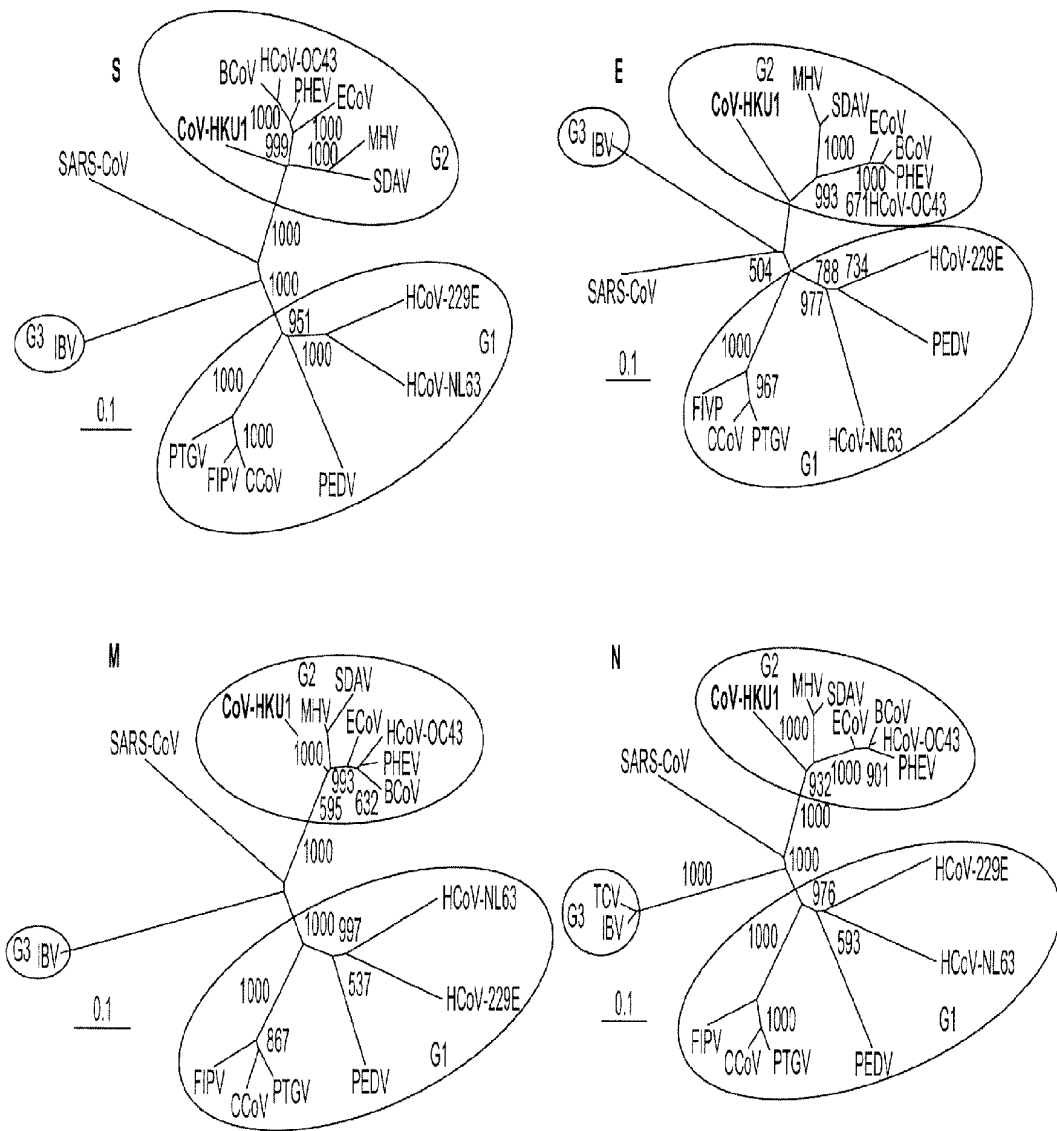


FIG. 5B

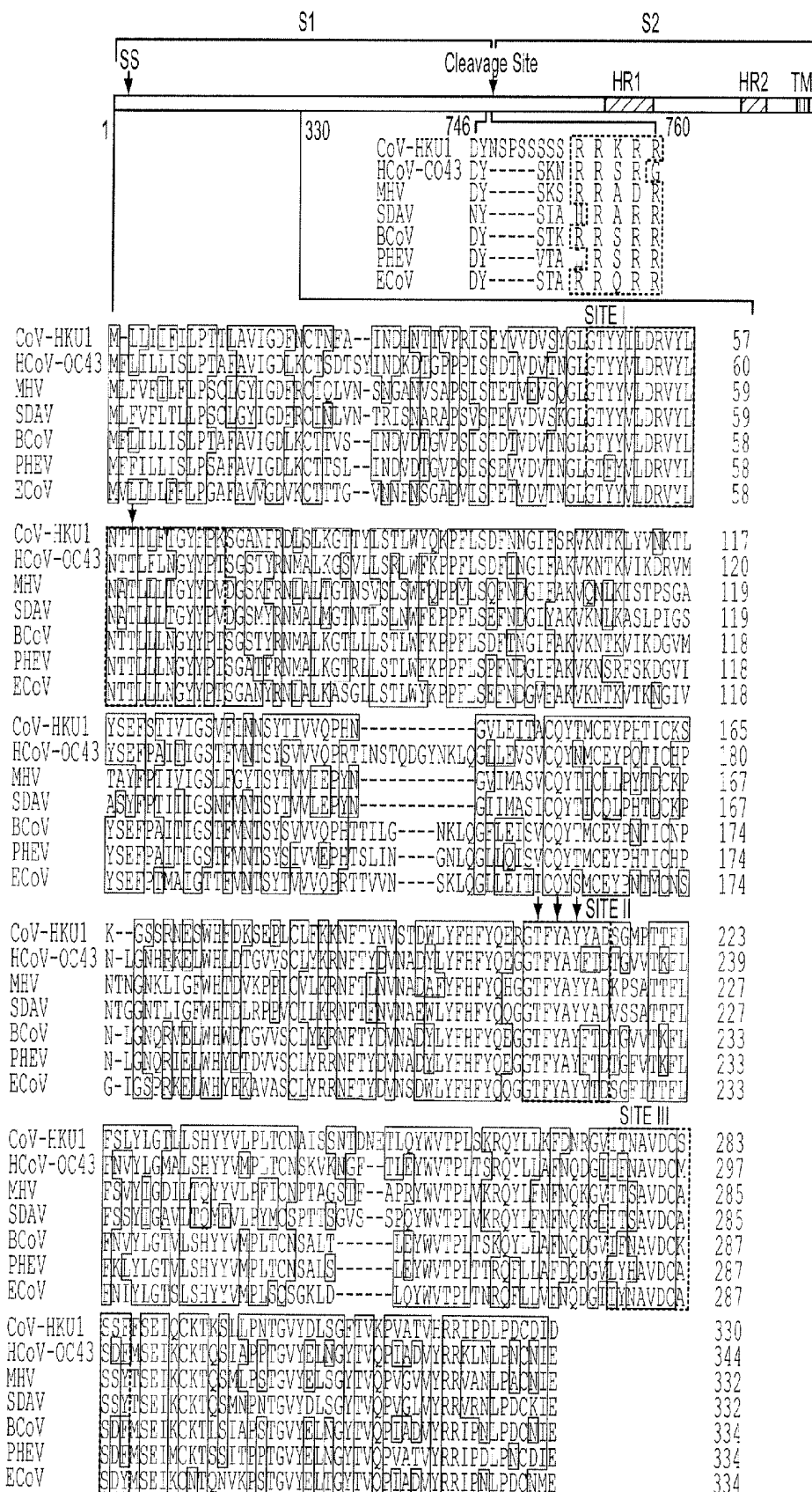


FIG. 6

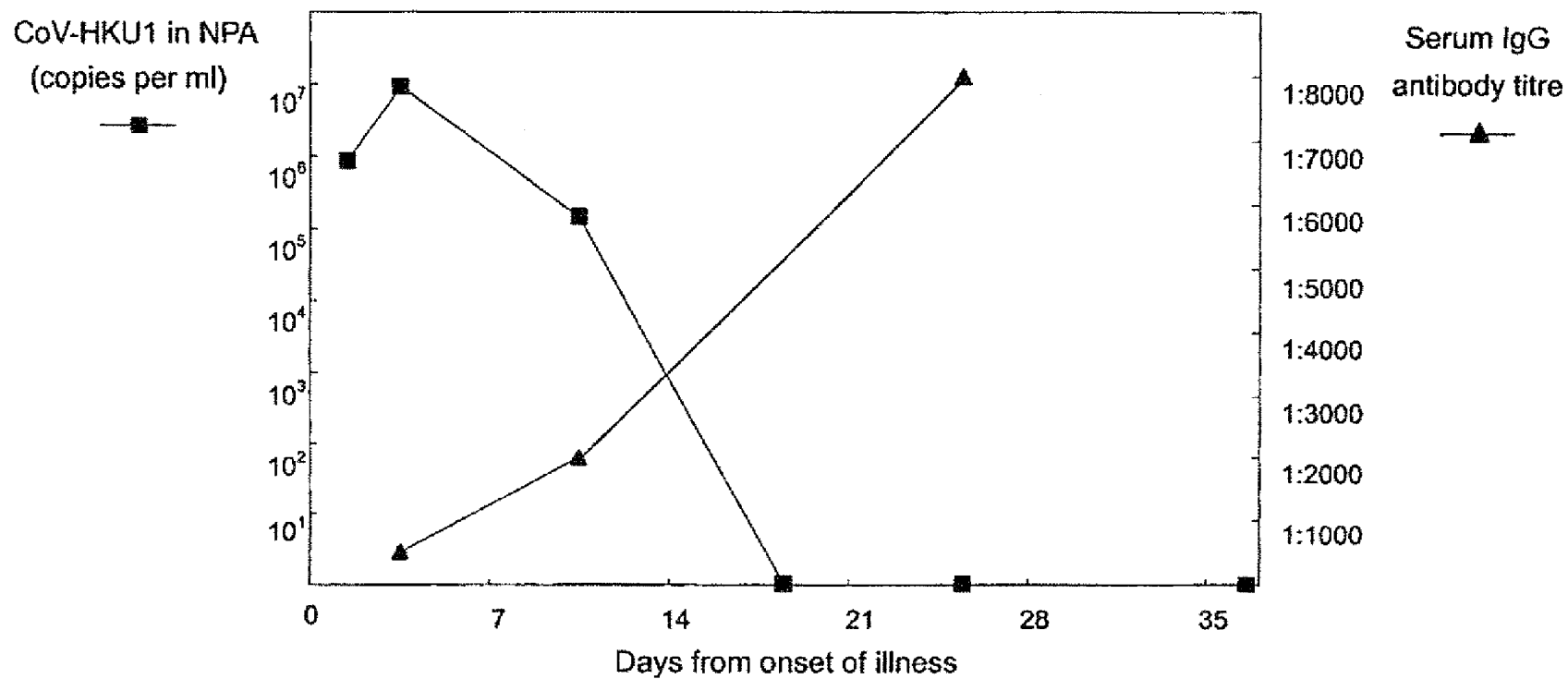


FIG. 7

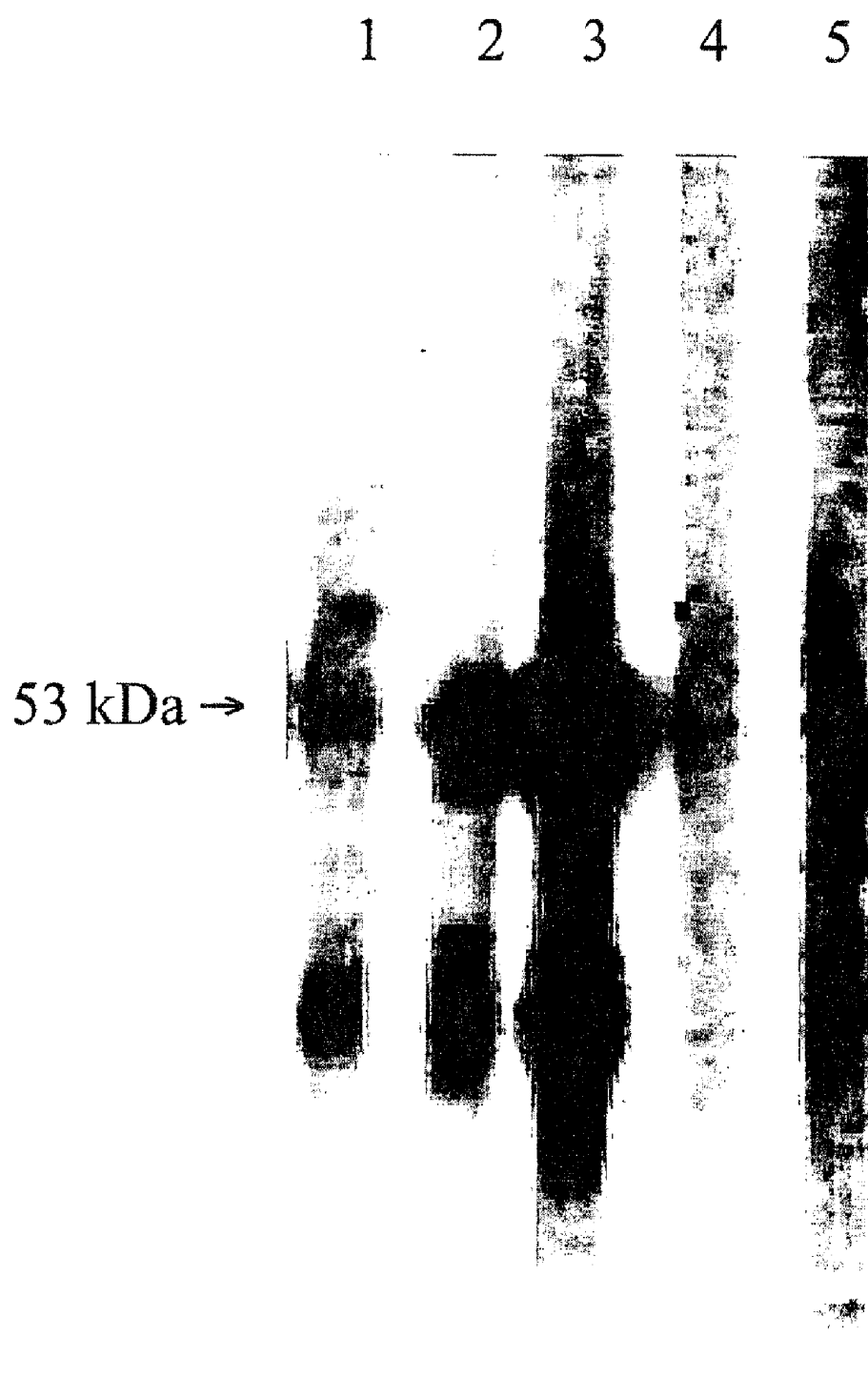


FIG. 8

NOVEL HUMAN VIRUS CAUSING RESPIRATORY TRACT INFECTION AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application is a continuation of U.S. application Ser. No. 10/895,064, filed Jul. 21, 2004, which is hereby incorporated by reference in its entirety.

SEQUENCE LISTING

[0002] The Sequence listing for this application is labeled "seq-list.txt", which was created on Jul. 21, 2004, and is 1,548 KB. The entire contents is incorporated herein by reference in its entirety.

1. INTRODUCTION

[0003] The present invention relates to a novel virus causing respiratory tract infection in 10 humans ["coronavirus-HKU1 (CoV-HKU1)"]. The CoV-HKU1 is identified to be phylogenetically similar to known members of Coronaviridae. The present invention relates to a nucleotide sequence comprising the complete genomic sequence or the CoV-HKU1. The invention further relates to nucleotide sequences comprising a portion of the genomic sequence of the CoV-HKU1. The invention also relates to the deduced amino acid sequences of the complete genome of the CoV-HKU1. The invention further relates to the nucleic acids and peptides encoded by and/or derived from these sequences and their use in diagnostic methods and therapeutic methods, such as for immunogens. The invention further encompasses chimeric or recombinant viruses encoded by said nucleotide sequences and antibodies directed against polypeptides encoded by the nucleotide sequence. Furthermore, the invention relates to vaccine preparations comprising the CoV-HKU1 recombinant and chimeric forms of said virus as well as protein extracts and subunits of said virus.

2. BACKGROUND OF THE INVENTION

[0004] In January, 2004, a 71-year-old Chinese man was admitted to hospital because of fever and chills for two days associated with sore throat, rhinorrhoea, productive cough with purulent sputum, headache and nausea. He had history of pulmonary tuberculosis more than 40 years ago complicated by cicatrization of right upper lobe and bronchiectasis with chronic *Pseudomonas aeruginosa* colonization of airways. He was a chronic smoker and also had chronic obstructive airway disease, hyperlipidemia, and asymptomatic abdominal aortic aneurysm. He had just returned from Shenzhen of China three days before admission. During his three-day trip to Shenzhen, he had no history of contact with or consumption of wild animals. On admission, his oral temperature was 37.6° C. Physical examination showed tracheal deviation to the right and inspiratory crackles over the anterior left lower zone. H is haemoglobin level was 14.7 g/dL, total white cell count $12.1 \times 10^9/L$, with neutrophil $9.7 \times 10^9/L$, lymphocyte $1.6 \times 10^9/L$ and monocyte $0.5 \times 10^9/L$, and plate count $303 \times 10^9/L$. His liver and renal function tests were within normal limits. Chest radiograph showed right upper lobe collapse and new patchy infiltrates over the left lower zone. Blood culture was performed. Empirical oral amoxicillin/clavulanate and azithromycin were commenced. Nasopharyngeal aspirates for direct antigen detection for res-

piratory viruses, RT-PCR for influenza A virus, human metapneumovirus and SARS-CoV, and viral cultures were negative. Sputum for bacterial culture only recovered *P. aeruginosa*. Sputum for mycobacterial culture was negative. Blood culture was negative. Paired sera for antibodies against *Mycoplasma*, *Chlamydia*, *Legionella*, and SARS-CoV did not show any rise in antibody titres. H is fever subsided two days after admission. H is cough improved and he was discharged after five days of hospitalization. Amoxicillin/clavulanate and azithromycin were continued for a total of seven days. The present inventors were the group involved in the investigation of this patient. All tests for identifying commonly recognized viruses and bacteria were negative in these patients. The etiologic agent responsible for this disease was not known until the complete genome of CoV-HKU1 from this patient by the present inventors as disclosed herein. Namely, the present invention discloses a novel human virus that has been identified from a patient suffering from pneumonia. The invention is useful in both clinical and scientific research applications.

3. SUMMARY OF INVENTION

[0005] The present invention is based upon the inventor's complete genome sequencing of a novel virus ("CoV-HKU1") causing pneumonia in humans. The virus was discovered from a patient suffering from pneumonia in Hong Kong. The virus is a single-stranded RNA virus of positive polarity which belongs to the order, Nidovirales, of the family, Coronaviridae. Accordingly, the invention relates to CoV-HKU1 that phylogenetically relates to known members of Coronaviridae. In a specific embodiment, the invention provides complete genomic sequence of CoV-HKU1. In a preferred embodiment, the virus comprises a nucleotide sequence of SEQ ID NO:1 and/or 3. In another specific embodiment, the invention provides nucleic acids isolated from the virus. The virus preferably comprises a nucleotide sequence of SEQ ID NO:1 and/or 3 in its genome. In a specific embodiment, the present invention provides isolated nucleic acid molecules comprising or, alternatively, consisting of the nucleotide sequence of SEQ ID NO:1, a complement thereof or a portion thereof, preferably at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO: 1, or a complement thereof. In another specific embodiment, the present invention provides isolated nucleic acid molecules comprising or, alternatively, consisting of the nucleotide sequence of SEQ ID NO:3, a complement thereof or a portion thereof, preferably at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1,000, 1,050, 1,100, 1,150, 1,200, 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 10,000, 11,000, 12,000, 13,000, 14,000, 15,000, 16,000, 17,000, 18,000, 19,000, 20,000, 21,000, 22,000, 23,000, 24,000, 25,000, 26,000, 27,000, 28,000, 29,000 or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:3, or a complement thereof. Furthermore, in another specific embodiment, the invention provides isolated nucleic acid molecules which hybridize under stringent conditions, as defined herein, to a nucleic acid molecule having the sequence of SEQ ID NO:1 or 3, or a complement thereof. In preferred embodiments, such nucleic acid molecules encode amino acid sequences that have biological activities exhibited by the polypeptides encoded by the nucleotide sequence of SEQ ID NO:1 or 3. In another specific embodiment, the

invention provides isolated polypeptides or proteins that are encoded by a nucleic acid molecule comprising or, alternatively consisting of a nucleotide sequence that is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:1, or a complement thereof. In yet another specific embodiment, the invention provides isolated polypeptides or proteins that are encoded by a nucleic acid molecule comprising or, alternatively consisting of a nucleotide sequence that is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1,000, 1,050, 1,100, 1,150, 1,200, 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 10,000, 11,000, 12,000, 13,000, 14,000, 15,000, 16,000, 17,000, 18,000, 19,000, 20,000, 21,000, 22,000, 23,000, 24,000, 25,000, 26,000, 27,000, 28,000, 29,000 or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:3, or a complement thereof. The polypeptides or proteins include those having the amino acid sequences of SEQ ID NO:2 and SEQ ID NOS:34-2918 shown in FIGS. 2 and 3, respectively. The invention further provides proteins or polypeptides that are isolated from the CoV-HKU1, including viral proteins isolated from cells infected with the virus but not present in comparable uninfected cells. The polypeptides or the proteins of the present invention preferably have a biological activity of the protein (including antigenicity and/or immunogenicity) encoded by the nucleotide sequence that is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:1. In other embodiments, the polypeptides or the proteins of the present invention have a biological activity of the protein (including antigenicity and/or immunogenicity) encoded by a nucleotide sequence that is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1,000, 1,050, 1,100, 1,150, 1,200, 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 10,000, 11,000, 12,000, 13,000, 14,000, 15,000, 16,000, 17,000, 18,000, 19,000, 20,000, 21,000, 22,000, 23,000, 24,000, 25,000, 26,000, 27,000, 28,000, 29,000 or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:3, or a complement thereof.

[0006] In one aspect, the invention relates to the use of CoV-HKU1 for diagnostic methods. In a specific embodiment, the invention provides a method of detecting in a biological sample an antibody that immunospecifically binds to the CoV-HKU1, or any proteins or polypeptides thereof. In another specific embodiment, the invention provides a method of detecting in a biological sample an antibody that immunospecifically binds to the CoV-HKU1-infected cells. In yet another specific embodiment, the invention provides a method of screening for an antibody that immunospecifically binds and neutralizes CoV-HKU1. Such an antibody is useful for a passive immunization or immunotherapy of a subject infected with CoV-HKU1.

[0007] The invention further relates to the use of the sequence information of the isolated virus for diagnostic methods. In a specific embodiment, the invention provides nucleic acid molecules which are suitable for use as primers consisting of or comprising the nucleotide sequence of SEQ ID NO:1 or 3, a complement thereof, or at least a portion of the nucleotide sequence thereof. In another specific embodiment, the invention provides nucleic acid molecules which are suitable for hybridization to CoV-HKU1 nucleic acid, including, but not limited to, as PCR primers, Reverse Tran-

scriptase primers, probes for Southern or Northern analysis or other nucleic acid hybridization analysis for the detection of CoV-HKU1 nucleic acids, e.g., consisting of or comprising the nucleotide sequence of SEQ ID NO:1 or 3, a complement thereof, or a portion thereof.

[0008] The invention further provides antibodies that specifically bind a polypeptide of the invention encoded by the nucleotide sequence of SEQ ID NO:1 or 3 or a fragment thereof, including the polypeptide having the amino acid sequence of SEQ ID NO:2 or SEQ ID NOS:34-2918 shown in FIGS. 2 and 3, or encoded by a nucleic acid comprising a nucleotide sequence that hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NO:1 or 3 and/or any CoV-HKU1 epitope, having one or more biological activities of a polypeptide of the invention. The invention further provides antibodies that specifically bind cells or tissues that are infected by CoV-HKU1. Such antibodies include, but are not limited to polyclonal, monoclonal, bi-specific, multi-specific, human, humanized, chimeric antibodies, single chain antibodies, Fab fragments, F(ab')₂ fragments, disulfide-linked Fvs, intrabodies and fragments containing either a VL or VH domain or even a complementary determining region (CDR) that specifically binds to a polypeptide of the invention.

[0009] In one embodiment, the invention provides methods for detecting the presence, activity or expression of the CoV-HKU1 of the invention in a biological material, such as cells, blood, saliva, urine, and so forth. The increased or decreased activity or expression of the CoV-HKU1 in a sample relative to a control sample can be determined by contacting the biological material with an agent which can detect directly or indirectly the presence, activity or expression of the CoV-HKU1. In a specific embodiment, the detecting agents are the antibodies or nucleic acid molecules of the present invention. Antibodies of the invention may also be used to detect and/or treat other coronaviruses, such as Severe Acute Respiratory Syndrome ("SARS") viruses.

[0010] In another embodiment, the invention provides vaccine preparations, comprising the CoV-HKU1 recombinant and chimeric forms of said virus, or protein subunits of the virus. In a specific embodiment, the present invention provides methods of preparing recombinant or chimeric forms of CoV-HKU1. In another specific invention, the vaccine preparations of the present invention comprise a nucleic acid or fragment of the CoV-HKU1, or nucleic acid molecules having the sequence of SEQ ID NO:1 or 3, or a fragment thereof. In another embodiment, the invention provides vaccine preparations comprising one or more polypeptides isolated from or produced from nucleic acid of CoV-HKU1. In a specific embodiment, the vaccine preparations comprise a polypeptide of the invention encoded by the nucleotide sequence of SEQ ID NO:1 or 3, or a fragment thereof, including the polypeptides having the amino acid sequences of SEQ ID NO:2 or SEQ ID NOS:34-2918 shown in FIGS. 2 and 3, respectively. Furthermore, the present invention provides methods for treating, ameliorating, managing or preventing respiratory tract infections caused by CoV-HKU1 by administering to a subject in need thereof the anti-viral agents of the present invention, alone or in combination with various anti-viral agents as well as adjuvants, and/or other pharmaceutically acceptable excipients.

[0011] In another aspect, the present invention provides methods for preventing or inhibiting, under a physiological condition, binding to a host cell, or infection of a host cell, or

replication in a host cell, of CoV-HKU1 or a virus comprising a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or 3 or a complement thereof, by administering to the host cell the anti-viral agents of the present invention, alone or in combination with other anti-viral agents. In a specific embodiment, the anti-viral agent of the invention includes the immunogenic preparations of the invention or an antibody that immunospecifically binds CoV-HKU1 or any CoV-HKU1 epitope and/or neutralizes CoV-HKU1. In another specific embodiment, the anti-viral agent is a polypeptide or protein of the present invention or a nucleic acid molecule of the invention. In a specific embodiment, the host cell is a mammalian cell, including a cell of human, primates, cows, horses, sheep, pigs, fowl (e.g., chickens), goats, cats, dogs, hamsters, mice and rats. Preferably a host cell is a primate cell, and most preferably a human cell. Furthermore, the present invention provides pharmaceutical compositions comprising anti-viral agents of the present invention and a pharmaceutically acceptable carrier. The invention also provides kits containing a pharmaceutical composition of the present invention.

3.1 Definitions

[0012] The term “an antibody or an antibody fragment that immunospecifically binds a polypeptide of the invention” as used herein refers to an antibody or a fragment thereof that immunospecifically binds to the polypeptide encoded by the nucleotide sequence of SEQ ID NO:1 or 3, or a fragment thereof, and does not non-specifically bind to other polypeptides. An antibody or a fragment thereof that immunospecifically binds to the polypeptide of the invention may cross-react with other antigens. Preferably, an antibody or a fragment thereof that immunospecifically binds to a polypeptide of the invention does not cross-react with other antigens. An antibody or a fragment thereof that immunospecifically binds to the polypeptide of the invention, can be identified by, for example, immunoassays or other techniques known to those skilled in the art.

[0013] An “isolated” or “purified” peptide or protein is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language “substantially free of cellular material” includes preparations of a polypeptide/protein in which the polypeptide/protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, a polypeptide/protein that is substantially free of cellular material includes preparations of the polypeptide/protein having less than about 30%, 20%, 10%, 5%, 2.5%, or 1%, (by dry weight) of contaminating protein. When the polypeptide/protein is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When polypeptide/protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, i.e., it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly, such preparations of the polypeptide/protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or compounds other than polypeptide/protein fragment of interest. In a preferred embodiment of the present invention, polypeptides/proteins are isolated or purified.

[0014] An “isolated” nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid molecule. Moreover, an “isolated” nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized. In a preferred embodiment of the invention, nucleic acid molecules encoding polypeptides/proteins of the invention are isolated or purified. The term “isolated” nucleic acid molecule does not include a nucleic acid that is a member of a library that has not been purified away from other library clones containing other nucleic acid molecules.

[0015] The term “portion” or “fragment” as used herein refers to a fragment of a nucleic acid molecule containing at least about 10, 15, 25, 30, 35, 40, 45, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 10,000, 11,000, 12,000, 13,000, 14,000, 15,000, 16,000, 17,000, 18,000, 19,000, 20,000, 21,000, 22,000, 23,000, 24,000, 25,000, 26,000, 27,000, 28,000, 29,000, or more contiguous nucleic acids in length of the relevant nucleic acid molecule and having at least one functional feature of the nucleic acid molecule (or the encoded protein has one functional feature of the protein encoded by the nucleic acid molecule); or a fragment of a protein or a polypeptide containing at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 90, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300, 320, 340, 360, 380, 400, 500, 600, 700, 800, 900, 1,000, 1,500, 2,000, 2,500, 3,000, 3,500, 4,000, 4,100, 4,200, 4,300, 4,350, 4,360, 4,370, 4,380 amino acid residues in length of the relevant protein or polypeptide and having at least one functional feature of the protein or polypeptide.

[0016] The term “having a biological activity of the protein” or “having biological activities of the polypeptides of the invention” refers to the characteristics of the polypeptides or proteins having a common biological activity similar or identical structural domain and/or having sufficient amino acid identity to the polypeptide encoded by the nucleotide sequence of SEQ ID NO:1 or 3, or the polypeptide having the amino acid sequence of SEQ ID NO:2, or a complement thereof. Such common biological activities of the polypeptides of the invention include antigenicity and immunogenicity.

[0017] The term “under stringent condition” refers to hybridization and washing conditions under which nucleotide sequences having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% identity to each other remain hybridized to each other. Such hybridization conditions are described in, for example but not limited to, Current Protocols in Molecular Biology, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6.; Basic Methods in Molecular Biology, Elsevier Science Publishing Co., Inc., N.Y. (1986), pp. 75-78, and 84-87; and Molecular Cloning, Cold Spring Harbor Laboratory, N.Y. (1982), pp. 387-389, and are well known to those skilled in the art. A preferred, non-limiting example of stringent hybridization conditions is hybridization in 6× sodium chloride/sodium citrate (SSC), 0.5% SDS at about 68° C. followed by one or more washes (e.g., about 5 to 30 min each) in 2×SSC, 0.5% SDS at room temperature. Another preferred, non-limiting example of stringent hybridization conditions is hybridization in 6×SSC at about 45° C.

followed by one or more washes (e.g., about 5 to 30 min each) in 0.2×SSC, 0.1% SDS at about 45–65° C.

[0018] The term “variant” as used herein refers either to a naturally occurring genetic mutant of CoV-HKU1 or a recombinantly prepared variation of CoV-HKU1 each of which contain one or more mutations in its genome compared to CoV-HKU1. The term “variant” may also refer either to a naturally occurring variation of a given peptide or a recombinantly prepared variation of a given peptide or protein in which one or more amino acid residues have been modified by amino acid substitution, addition, or deletion.

4. DESCRIPTION OF FIGURES

[0019] FIG. 1 shows a partial DNA sequence (SEQ ID NO:1) and its deduced amino acid sequence (SEQ ID NO:2) obtained from CoV-HKU1 that has 91% amino acid identity to the RNA-dependent RNA polymerase protein of known Coronaviruses.

[0020] FIG. 2 shows the entire genomic DNA sequence (SEQ ID NO:3) of CoV-HKU1 and its deduced amino acid sequences therefrom in three frames. An asterisk (*) indicates a stop codon which marks the end of a peptide. The first-frame translation and amino acid sequences: SEQ ID NOS:34-456; the second-frame translation and amino acid sequences: SEQ ID NOS:457-723; and the third-frame translation and amino acid sequences: SEQ ID NOS:724-1318.

[0021] FIG. 3 shows the complement (SEQ ID NO: 1319) of the entire genomic DNA sequence (SEQ ID NO:3) of CoV-HKU1 in 3'→5' orientation and its deduced amino acid sequences therefrom in three frames. An asterisk (*) indicates a stop codon which marks the end of a peptide. The first-frame translation and amino acid sequences: SEQ ID NOS:1319-1907; the second-frame translation and amino acid sequences: SEQ ID NO:1908-2453; and the third-frame translation and amino acid sequences: SEQ ID NOS:2454-2918.

[0022] FIG. 4 shows the genome organization of CoV-HKU1. Arrows indicate the putative cleavage sites of the polyprotein encoded by ORF 1a and ORF 1b. The peptides are shown in SEQ ID NOS:15-17, respectively, in order of appearance.

[0023] FIG. 5A shows the phylogenetic analysis of the chymotrypsin like protease (3CL^{pro}), replicase (Rep), helicase (Hel), and hemagglutinin esterase (HE); and FIG. 5B shows that of the spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins of CoV-HKU1. The trees were constructed by the neighbor joining method using the Jukes-Cantor correction and bootstrap values were calculated from 1000 trees. A total of 303, 928, 603, 386, 1356, 82, 223 and 441 amino acid positions in 3CL^{pro}, Rep, Hel, HE, S, E, M, and N respectively were included in the analysis. The scale bar indicates the estimated number of substitutions per 10 amino acids.

[0024] FIG. 6 shows the important features of the S protein of CoV-HKU1 (residues 7-336 of SEQ ID NO:420) in comparison with those of other viruses, i.e., HCoV-OC43 (human coronavirus OC43; SEQ ID NO:21), MHV (murine hepatitis virus; SEQ ID NO:22), SDAV (rat sialodacryoadenitis encephalomyelitis virus; SEQ ID NO:23), BCoV (bovine coronavirus; SEQ ID NO:24), PHEV (porcine hemagglutinating encephalomyelitis virus; SEQ ID NO:25), and ECoV (equine coronavirus; SEQ ID NO:26). The cleavage site peptides are shown in residues 752-766 of SEQ ID NO:420 and SEQ ID NOS:28-33, respectively, in order of appearance.

[0025] FIG. 7 shows the sequential quantitative RT-PCR (closed squares; copies/ml) for CoV-HKU1 in nasopharyngeal aspirates; and serum IgG antibody titers against N protein of CoV-HKU1 (closed triangles).

[0026] FIG. 8 shows the Western blot analysis of purified recombinant CoV-HKU1 N protein antigen. Prominent immunoreactive protein bands of about 53 kDa were detected by the Western blot using the patient's sera obtained during the second and fourth weeks of the illness (lanes 2 and 3). Only very faint bands were observed with the serum samples obtained from the patient during the first week of the illness (lane 1) and two healthy blood donors (lane 4 and 5), respectively.

5. DETAILED DESCRIPTION OF THE INVENTION

[0027] The present invention relates to the CoV-HKU1 that phylogenetically relates to known Coronaviruses. In a specific embodiment, CoV-HKU1 comprises a nucleotide sequence of SEQ ID NO:1 and/or 3. In a specific embodiment, the present invention provides isolated nucleic acid molecules of the CoV-HKU1, comprising, or, alternatively, consisting of the nucleotide sequence of SEQ ID NO:1 and/or 3, a complement thereof or a portion thereof. In another specific embodiment, the invention provides isolated nucleic acid molecules which hybridize under stringent conditions, as defined herein, to a nucleic acid molecule having the sequence of SEQ ID NO:1 or 3, or specific genes of known member of Coronaviridae, or a complement thereof. In another specific embodiment, the invention provides isolated polypeptides or proteins that are encoded by a nucleic acid molecule comprising a nucleotide sequence that is at least about 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:1, or a complement thereof. In yet another specific embodiment, the invention provides isolated polypeptides or proteins that are encoded by a nucleic acid molecule comprising or, alternatively consisting of a nucleotide sequence that is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1,000, 1,050, 1,100, 1,150, 1,200, 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 10,000, 11,000, 12,000, 13,000, 14,000, 15,000, 16,000, 17,000, 18,000, 19,000, 20,000, 21,000, 22,000, 23,000, 24,000, 25,000, 26,000, 27,000, 28,000, 29,000 or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:3, or a complement thereof. The polypeptides or the proteins of the present invention preferably have one or more biological activities of the proteins encoded by the sequence of SEQ ID NO:1, 3, or the native viral proteins containing the amino acid sequences encoded by the sequence of SEQ ID NO:1 or 3.

[0028] The invention further relates to the use of the sequence information of the isolated virus for diagnostic and therapeutic methods. In a specific embodiment, the invention provides the entire nucleotide sequence of CoV-HKU1 (SEQ ID NO:3), or fragments, or complement thereof. Furthermore, the present invention relates to a nucleic acid molecule that hybridizes any portion of the genome of the CoV-HKU1 (SEQ ID NO:3) under the stringent conditions. In a specific embodiment, the invention provides nucleic acid molecules which are suitable for use as primers consisting of or comprising the nucleotide sequence of SEQ ID NO:1 or 3, or a complement thereof, or a portion thereof. In another specific embodiment, the invention provides nucleic acid molecules

which are suitable for use as hybridization probes for the detection of nucleic acids encoding a polypeptide of the invention, consisting of or comprising the nucleotide sequence of SEQ ID NO:1 or 3, a complement thereof, or a portion thereof. The invention further encompasses chimeric or recombinant viruses or viral proteins encoded by said nucleotide sequences.

[0029] The invention further provides antibodies that specifically bind a polypeptide of the invention encoded by the nucleotide sequence of SEQ ID NO:1 or 3, or a fragment thereof, or any CoV-HKU1 epitope as well as the polypeptides having the amino acid sequences of SEQ ID NO:2 and SEQ ID NOS:34-2918, respectively, shown in FIGS. 2 and 3. Such antibodies include, but are not limited to polyclonal, monoclonal, bi-specific, multi-specific, human, humanized, chimeric antibodies, single chain antibodies, Fab fragments, F(ab')₂ fragments, disulfide-linked Fvs, intrabodies and fragments containing either a VL or VH domain or even a complementary determining region (CDR) that specifically binds to a polypeptide of the invention.

[0030] In one embodiment, the invention provides methods for detecting the presence, activity or expression of the CoV-HKU1 of the invention in a biological material, such as cells, blood, saliva, urine, sputum, nasopharyngeal aspirates, and so forth. The presence of the CoV-HKU1 in a sample can be determined by contacting the biological material with an agent which can detect directly or indirectly the presence, activity or expression of the CoV-HKU1. In a specific embodiment, the detection agents are the antibodies of the present invention. In another embodiment, the detection agent is a nucleic acid of the present invention.

[0031] In another embodiment, the invention provides vaccine preparations comprising the CoV-HKU1 recombinant and chimeric forms of said virus, or subunits of the virus.

[0032] The present invention further provides methods of preparing recombinant or chimeric forms of CoV-HKU1. In another specific embodiment, the vaccine preparations of the present invention comprise one or more nucleic acid molecules comprising or consisting of the sequence of SEQ ID NO:1 and/or 3, or a fragment thereof. In another embodiment, the invention provides vaccine preparations comprising one or more polypeptides of the invention encoded by a nucleotide sequence comprising or consisting of the nucleotide sequence of SEQ ID NO:1 and/or 3, or a fragment thereof, including the polypeptides having the amino acid sequences of SEQ ID NO:2 or SEQ ID NOS:34-2918 shown in FIGS. 2 and 8. Furthermore, the present invention provides methods for treating, ameliorating, managing, or preventing respiratory tract infections by administering to a subject in need thereof the anti-viral agents of the present invention, alone or in combination with other antivirals [e.g., amantadine, rimantadine, gancyclovir, acyclovir, ribavirin, penciclovir, oseltamivir, foscarnet zidovudine (AZT), didanosine (ddI), lamivudine (3TC), zalcitabine (ddC), stavudine (d4T), nevirapine, delavirdine, indinavir, ritonavir, vidarabine, nelfinavir, saquinavir, relenza, tamiflu, pleconaril, interferons, etc.], steroids and corticosteroids such as prednisone, cortisone, fluticasone and glucocorticoid, antibiotics, analgesics, bronchodilators, or other treatments for respiratory and/or viral infections. In one aspect, the anti-viral agent of the present invention prevents or inhibits the binding of the virus or viral proteins to a host cell under a physiological condition, thereby preventing or inhibiting the infection of the host cell by the virus. In another aspect, the anti-viral agent of the

invention prevents or inhibits replication of the viral nucleic acid molecules in the host cell under a physiological condition by interacting with the viral nucleic acid molecules or its transcription mechanisms. In a specific embodiment, the anti-viral agent of the invention includes the vaccine or immunogenic preparations of the invention or an antibody that immunospecifically binds CoV-HKU1 or any CoV-HKU1 epitope and may neutralizes CoV-HKU1. In another specific embodiment, the anti-viral agent is a polypeptide or protein of the invention or a nucleic acid molecule of the invention. In addition, the present invention provides a method of preventing or inhibiting replication in a host cell of a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1 and/or 3, or inhibiting the activities of the polypeptides encoded by the nucleotide sequence of SEQ ID NO:1 and/or 3, a complement thereof, or a portion thereof, including the polypeptides having the amino acid sequence of SEQ ID NO:2 or SEQ ID NOS:34-2918 shown in FIGS. 2 and 8, by administering to said host cell the anti-viral agent of the invention. In a specific embodiment the host cell is a mammalian cell, such as a cell of humans, primates, horses, cows, sheep, pigs, goats, dogs, cats, avian species and rodents. Preferably, the cell is a primate cell and most preferably a human cell.

[0033] Furthermore, the present invention provides pharmaceutical compositions comprising anti-viral agents of the present invention and a pharmaceutically acceptable carrier. The present invention also provides kits comprising pharmaceutical compositions of the present invention.

5.1 Recombinant and Chimeric CoV-HKU1

[0034] The present invention encompasses recombinant or chimeric viruses encoded by viral vectors derived from the genome of CoV-HKU1 or natural variants thereof. In a specific embodiment, a recombinant virus is one derived from the CoV-HKU1. In a specific embodiment, the virus has a nucleotide sequence of SEQ ID NO:3. In another specific embodiment, a recombinant virus is one derived from a natural variant of CoV-HKU1. A natural variant of CoV-HKU1 has a sequence that is different from the genomic sequence (SEQ ID NO:3) of CoV-HKU1, due to one or more naturally occurred mutations, including, but not limited to, point mutations, rearrangements, insertions, deletions etc., to the genomic sequence that may or may not result in a phenotypic change. In accordance with the present invention, a viral vector which is derived from the genome of the CoV-HKU1, is one that contains a nucleic acid sequence that encodes at least a part of one ORF of the CoV-HKU1. In a specific embodiment, the ORF comprises or consists of a nucleotide sequence of SEQ ID NO:1 or a fragment thereof. In a specific embodiment, there are more than one ORF within the nucleotide sequence of SEQ ID NO:3, or a fragment thereof. In another embodiment, the polypeptides encoded by the ORF comprises or consists of amino acid sequences of SEQ ID NOS:34-2918 shown in FIGS. 2 and 8, or SEQ ID NO:2, or a fragment thereof. In accordance with the present invention these viral vectors may or may not include nucleic acids that are non-native to the viral genome.

[0035] In another specific embodiment, a chimeric virus of the invention is a recombinant CoV-HKU1 which further comprises a heterologous nucleotide sequence. In accordance with the invention, a chimeric virus may be encoded by a nucleotide sequence in which heterologous nucleotide sequences have been added to the genome or in which endog-

enous or native nucleotide sequences have been replaced with heterologous nucleotide sequences.

[0036] According to the present invention, the chimeric viruses are encoded by the viral vectors of the invention which further comprise a heterologous nucleotide sequence. In accordance with the present invention a chimeric virus is encoded by a viral vector that may or may not include nucleic acids that are non-native to the viral genome. In accordance with the invention a chimeric virus is encoded by a viral vector to which heterologous nucleotide sequences have been added, inserted or substituted for native or non-native sequences. In accordance with the present invention, the chimeric virus may be encoded by nucleotide sequences derived from different strains or variants of CoV-HKU1. In particular, the chimeric virus is encoded by nucleotide sequences that encode antigenic polypeptides derived from different strains or variants of CoV-HKU1.

[0037] A chimeric virus may be of particular use for the generation of recombinant vaccines protecting against two or more viruses (Tao et al., J. Virol. 72, 2955-2961; Durbin et al., 2000, J. Virol. 74, 6821-6831; Skiadopoulos et al., 1998, J. Virol. 72, 1762-1768 (1998); Teng et al., 2000, J. Virol. 74, 9317-9321). For example, it can be envisaged that a virus vector derived from the CoV-HKU1 expressing one or more proteins of variants of CoV-HKU1, or vice versa, will protect a subject vaccinated with such vector against infections by both the native CoV-HKU1 and the variant. Attenuated and replication-defective viruses may be of use for vaccination purposes with live vaccines as has been suggested for other viruses.

[0038] In accordance with the present invention the heterologous sequence to be incorporated into the viral vectors encoding the recombinant or chimeric viruses of the invention include sequences obtained or derived from different strains or variants of CoV-HKU1.

[0039] In certain embodiments, the chimeric or recombinant viruses of the invention are encoded by viral vectors derived from viral genomes wherein one or more sequences, intergenic regions, termini sequences, or portions or entire ORE have been substituted with a heterologous or non-native sequence. In certain embodiments of the invention, the chimeric viruses of the invention are encoded by viral vectors derived from viral genomes wherein one or more heterologous sequences have been inserted or added to the vector.

[0040] The selection of the viral vector may depend on the species of the subject that is to be treated or protected from a viral infection.

[0041] In accordance with the present invention, the viral vectors can be engineered to provide antigenic sequences which confer protection against infection by the CoV-HKU1 and natural variants thereof. The viral vectors may be engineered to provide one, two, three or more antigenic sequences. In accordance with the present invention the antigenic sequences may be derived from the same virus, from different strains or variants of the same type of virus, or from different viruses.

[0042] The expression products and/or recombinant or chimeric virions obtained in accordance with the invention may advantageously be utilized in vaccine formulations. The expression products and chimeric virions of the present invention may be engineered to create vaccines against a broad range of pathogens, including viral and bacterial antigens, tumor antigens, allergen antigens, and auto antigens involved in autoimmune disorders. In particular, the chimeric

virions of the present invention may be engineered to create vaccines for the protection of a subject from infections with CoV-HKU1 and variants thereof.

[0043] In certain embodiments, the expression products and recombinant or chimeric virions of the present invention may be engineered to create vaccines against a broad range of pathogens, including viral antigens, tumor antigens and autoantigens involved in autoimmune disorders. One way to achieve this goal involves modifying existing CoV-HKU1 genes to contain foreign sequences in their respective external domains. Where the heterologous sequences are epitopes or antigens of pathogens, these chimeric viruses may be used to induce a protective immune response against the disease agent from which these determinants are derived.

[0044] Thus, the present invention relates to the use of viral vectors and recombinant or chimeric viruses to formulate vaccines against a broad range of viruses and/or antigens. The present invention also encompasses recombinant viruses comprising a viral vector derived from the CoV-HKU1 or variants thereof which contains sequences which result in a virus having a phenotype more suitable for use in vaccine formulations. The mutations and modifications can be in coding regions, in intergenic regions and in the leader and trailer sequences of the virus.

[0045] The invention provides a host cell comprising a nucleic acid or a vector according to the invention. Plasmid or viral vectors containing the polymerase components of CoV-HKU1 are generated in prokaryotic cells for the expression of the components in relevant cell types (bacteria, insect cells, eukaryotic cells). Plasmid or viral vectors containing full-length or partial copies of the CoV-HKU1 genome will be generated in prokaryotic cells for the expression of viral nucleic acids in-vitro or in-vivo. The latter vectors may contain other viral sequences for the generation of chimeric viruses or chimeric virus proteins, may lack parts of the viral genome for the generation of replication defective virus, and may contain mutations, deletions or insertions for the generation of attenuated viruses.

[0046] In addition, eukaryotic cells, transiently or stably expressing one or more full-length or partial CoV-HKU1 proteins can be used. Such cells can be made by transfection (proteins or nucleic acid vectors), infection (viral vectors) or transduction (viral vectors) and may be useful for complementation of mentioned wild type, attenuated, replication-defective or chimeric viruses.

[0047] The viral vectors and chimeric viruses of the present invention may be used to modulate a subject's immune system by stimulating a humoral immune response, a cellular immune response or by stimulating tolerance to an antigen. As used herein, a subject means: humans, primates, horses, cows, sheep, pigs, goats, dogs, cats, avian species and rodents.

5.2 Formulation of Vaccines and Antivirals

[0048] In a preferred embodiment, the invention provides a proteinaceous molecule or CoV-HKU1 specific viral protein or functional fragment thereof encoded by a nucleic acid according to the invention. Useful proteinaceous molecules are for example derived from any of the genes or genomic fragments derivable from the virus according to the invention, including envelop protein (E protein), integral membrane protein (M protein), spike protein (S protein), nucleocapsid protein (N protein), hemagglutinin esterase (HE protein), and RNA-dependent RNA polymerase. Such molecules, or anti-

genic fragments thereof, as provided herein, are for example useful in diagnostic methods or kits and in pharmaceutical compositions such as subunit vaccines. Particularly useful are polypeptides encoded by the nucleotide sequence of SEQ ID NO:1 or 3, including the polypeptides having the amino acid sequences of SEQ ID NOS:34-2918 in FIGS. 2 and 8, or SEQ ID NO:2, or antigenic fragments thereof for inclusion as antigen or subunit immunogen, but inactivated whole virus can also be used. Particularly useful are also those proteinaceous substances that are encoded by recombinant nucleic acid fragments of the CoV-HKU1 genome; of course preferred are those that are within the preferred bounds and metes of ORFs, in particular, for eliciting CoV-HKU1 specific antibody or T cell responses, whether in vivo (e.g. for protective or therapeutic purposes or for providing diagnostic antibodies) or in vitro (e.g. by phage display technology or another technique useful for generating synthetic antibodies).

[0049] The invention provides vaccine formulations for the prevention and treatment of infections with CoV-HKU1. In certain embodiments, the vaccine of the invention comprises recombinant and chimeric viruses of the CoV-HKU1.

[0050] In another aspect, the present invention also provides DNA vaccine formulations comprising a nucleic acid or fragment of the CoV-HKU1, or nucleic acid molecules having the sequence of SEQ ID NO:1 or 3, or a fragment thereof. In another specific embodiment, the DNA vaccine formulations of the present invention comprises a nucleic acid or fragment thereof encoding the antibodies which immunospecifically binds CoV-HKU1. In DNA vaccine formulations, a vaccine DNA comprises a viral vector, such as that derived from the CoV-HKU1, bacterial plasmid, or other expression vector, bearing an insert comprising a nucleic acid molecule of the present invention operably linked to one or more control elements, thereby allowing expression of the vaccinating proteins encoded by said nucleic acid molecule in a vaccinated subject. Such vectors can be prepared by recombinant DNA technology as recombinant or chimeric viral vectors carrying a nucleic acid molecule of the present invention.

[0051] Various heterologous vectors are described for DNA vaccinations against viral infections. For example, the vectors described in the following references may be used to express CoV-HKU1 sequences instead of the sequences of the viruses or other pathogens described; in particular, vectors described for hepatitis B virus (Michel, M. L. et al., 1995, DAN-mediated immunization to the hepatitis B surface antigen in mice: Aspects of the humoral response mimic hepatitis B viral infection in humans, *Proc. Natl. Acad. Sci. USA* 92:5307-5311; Davis, H. L. et al., 1993, DNA-based immunization induces continuous secretion of hepatitis B surface antigen and high levels of circulating antibody, *Human Molec. Genetics* 2:1847-1851), HIV virus (Wang, B. et al., 1993, Gene inoculation generates immune responses against human immunodeficiency virus type 1, *Proc. Natl. Acad. Sci. USA* 90:4156-4160; Lu, S. et al., 1996, Simian immunodeficiency virus DNA vaccine trial in macaques, *J. Virol.* 70:3978-3991; Letvin, N. L. et al., 1997, Potent, protective anti-HIV immune responses generated by bimodal HIV envelope DNA plus protein vaccination, *Proc Natl Acad Sci USA* 94(17): 9378-83), and influenza viruses (Robinson, H L et al., 1993, Protection against a lethal influenza virus challenge by immunization with a haemagglutinin-expressing plasmid DNA, *Vaccine* 11:957-960; Ulmer, J. B. et al., Heterologous protection against influenza by injection of DNA encoding a viral protein, *Science* 259:1745-1749), as well as bacterial infec-

tions, such as tuberculosis (Tascon, R. E. et al., 1996, Vaccination against tuberculosis by DNA injection, *Nature Med.* 2:888-892; Huygen, K. et al., 1996, Immunogenicity and protective efficacy of a tuberculosis DNA vaccine, *Nature Med.* 2:893-898), and parasitic infection, such as malaria (Sedegah, M., 1994, Protection against malaria by immunization with plasmid DNA encoding circumsporozoite protein, *Proc. Natl. Acad. Sci. USA* 91:9866-9870; Doolan, D. L. et al., 1996, Circumventing genetic restriction of protection against malaria with multigene DNA immunization: CD8+ T cell-interferon γ , and nitric oxide-dependent immunity, *J. Exper. Med.*, 1183:1739-1746).

[0052] Many methods may be used to introduce the vaccine formulations described above. These include, but are not limited to, oral, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, and intranasal routes. Alternatively, it may be preferable to introduce the chimeric virus vaccine formulation via the natural route of infection of the pathogen for which the vaccine is designed. The DNA vaccines of the present invention may be administered in saline solutions by injections into muscle or skin using a syringe and needle (Wolff J. A. et al., 1990, Direct gene transfer into mouse muscle in vivo, *Science* 247:1465-1468; Raz, E., 1994, Intradermal gene immunization: The possible role of DNA uptake in the induction of cellular immunity to viruses, *Proc. Natl. Acad. Sci. USA* 91:9519-9523). Another way to administer DNA vaccines is called "gene gun" method, whereby microscopic gold beads coated with the DNA molecules of interest is fired into the cells (Tang, D. et al., 1992, Genetic immunization is a simple method for eliciting an immune response, *Nature* 356:152-154). For general reviews of the methods for DNA vaccines, see Robinson, H. L., 1999, DNA vaccines: basic mechanism and immune responses (Review), *Int. J. Mol. Med.* 4(5):549-555; Barber, B., 1997, Introduction: Emerging vaccine strategies, *Seminars in Immunology* 9(5):269-270; and Robinson, H. L. et al., 1997, DNA vaccines, *Seminars in Immunology* 9(5):271-283.

5.3 Adjuvants and Carrier Molecules

[0053] CoV-HKU1-associated antigens are administered with one or more adjuvants. In one embodiment, the CoV-HKU1-associated antigen is administered together with a mineral salt adjuvants or mineral salt gel adjuvant. Such mineral salt and mineral salt gel adjuvants include, but are not limited to, aluminum hydroxide (ALHYDROGEL, REHYDRAGEL), aluminum phosphate gel, aluminum hydroxyphosphate (ADJU-PHOS), and calcium phosphate.

[0054] In another embodiment, CoV-HKU1-associated antigen is administered with an immunostimulatory adjuvant. Such class of adjuvants, include, but are not limited to, cytokines (e.g., interleukin-2, interleukin-7, interleukin-12, granulocyte-macrophage colony stimulating factor (GM-CSF), interferon- γ interleukin-1 β (IL-1 β), and IL-1 β peptide or Sclavo Peptide), cytokine-containing liposomes, triterpenoid glycosides or saponins (e.g., QuilA and QS-21, also sold under the trademark STIMULON, ISCOPREP), Muramyl Dipeptide (MDP) derivatives, such as N-acetyl-muramyl-L-threonyl-D-isoglutamine (Threonyl-MDP, sold under the trademark TERMURTIDE), GMDP, N-acetyl-nor-muramyl-L-alanyl-D-isoglutamine, N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3-hydroxy phosphoryloxy)-ethylamine, muramyl tripeptide phosphatidylethanolamine (MTP-PE), unmethylated CpG dinucleotides and oligonucleotides, such as bacterial DNA

and fragments thereof, LPS, monophosphoryl Lipid A (3D-MLA sold under the trademark MPL), and polyphosphazenes.

[0055] In another embodiment, the adjuvant used is a particular adjuvant, including, but not limited to, emulsions, e.g., Freund's Complete Adjuvant, Freund's Incomplete Adjuvant, squalene or squalene oil-in-water adjuvant formulations, such as SAF and MF59, e.g., prepared with block-copolymers, such as L-121 (polyoxypropylene/polyoxyethylene) sold under the trademark PLURONIC L-121, Liposomes, Virosomes, cochleates, and immune stimulating complex, which is sold under the trademark ISCOM.

[0056] In another embodiment, a microparticulate adjuvant is used. Microparticulate adjuvants include, but are not limited to biodegradable and biocompatible polyesters, homo- and copolymers of lactic acid (PLA) and glycolic acid (PGA), poly(lactide-co-glycolides) (PLGA) microparticles, polymers that self-associate into particulates (poloxamer particles), soluble polymers (polyphosphazenes), and virus-like particles (VLPs) such as recombinant protein particulates, e.g., hepatitis B surface antigen (HbsAg).

[0057] Yet another class of adjuvants that may be used include mucosal adjuvants, including but not limited to heat-labile enterotoxin from *Escherichia coli* (LT), cholera holotoxin (CT) and cholera Toxin B Subunit (CTB) from *Vibrio cholerae*, mutant toxins (e.g., LTK63 and LTR72), microparticles, and polymerized liposomes.

[0058] In other embodiments, any of the above classes of adjuvants may be used in combination with each other or with other adjuvants. For example, non-limiting examples of combination adjuvant preparations that can be used to administer the CoV-HKU1-associated antigens of the invention include liposomes containing immunostimulatory protein, cytokines, or T-cell and/or B-cell peptides, or microbes with or without entrapped IL-2 or microparticles containing enterotoxin. Other adjuvants known in the art are also included within the scope of the invention (see *Vaccine Design: The Subunit and Adjuvant Approach*, Chap. 7, Michael F. Powell and Mark J. Newman (eds.), Plenum Press, New York, 1995, which is incorporated herein in its entirety).

[0059] The effectiveness of an adjuvant may be determined by measuring the induction of antibodies directed against an immunogenic polypeptide containing a CoV-HKU1 polypeptide epitope, the antibodies resulting from administration of this polypeptide in vaccines which are also comprised of the various adjuvants.

[0060] The polypeptides may be formulated into the vaccine as neutral or salt forms. Pharmaceutically acceptable salts include the acid additional salts (formed with free amino groups of the peptide) and which are formed with inorganic acids, such as, for example, hydrochloric or phosphoric acids, or organic acids such as acetic, oxalic, tartaric, maleic, and the like. Salts formed with free carboxyl groups may also be derived from inorganic bases, such as, for example, sodium potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine and the like.

[0061] The vaccines of the invention may be multivalent or univalent. Multivalent vaccines are made from recombinant viruses that direct the expression of more than one antigen.

[0062] Many methods may be used to introduce the vaccine formulations of the invention; these include but are not limited to oral, intradermal, intramuscular, intraperitoneal, intra-

venous, subcutaneous, intranasal routes, and via scarification (scratching through the top layers of skin, e.g., using a bifurcated needle).

[0063] The patient to which the vaccine is administered is preferably a mammal, most preferably a human, but can also be a non-human animal including but not limited to cows, horses, sheep, pigs, fowl (e.g., chickens), goats, cats, dogs, hamsters, mice and rats.

5.4 Preparation of Antibodies

[0064] Antibodies which specifically recognize a polypeptide of the invention, such as, but not limited to, polypeptides comprising the sequence of SEQ ID NO:2 or any of SEQ ID NOS: 34-2918 or CoV-HKU1 epitope, or antigen-binding fragments thereof, can be used for detecting, screening, and isolating the polypeptide of the invention or fragments thereof, or similar sequences that might encode similar enzymes from the other organisms. For example, in one specific embodiment, an antibody which immunospecifically binds CoV-HKU1 epitope, or a fragment thereof, can be used for various in vitro detection assays, including enzyme-linked immunosorbent assays (ELISA), radioimmunoassays, Western blot, etc., for the detection of a polypeptide of the invention or, preferably, CoV-HKU1, in samples, for example, a biological material, including cells, cell culture media (e.g., bacterial cell culture media, mammalian cell culture media, insect cell culture media, yeast cell culture media, etc.), blood, plasma, serum, tissues, sputum, nasopharyngeal aspirates, etc.

[0065] Antibodies specific for a polypeptide of the invention or any epitope of CoV-HKU1 may be generated by any suitable method known in the art. Polyclonal antibodies to an antigen-of-interest, for example, the CoV-HKU1 epitopes or polypeptides encoded by a nucleotide sequence of SEQ ID NO:1 or 3, including the polypeptides shown in FIG. 2 (SEQ ID NOS:34-1318), FIG. 8 (SEQ ID NOS:1319-2918), as well as SEQ ID NO:2, can be produced by various procedures well known in the art. For example, an antigen can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc., to induce the production of antisera containing polyclonal antibodies specific for the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete) adjuvant, mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful adjuvants for humans such as BCG (Bacille Calmette-Guerin) and *Corynebacterium parvum*. Such adjuvants are also well known in the art (see Section 5.4, supra).

[0066] Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques including those known in the art and taught, for example, in Harlow et al., *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: *Monoclonal Antibodies and T-Cell Hybridomas*, pp. 563-681 (Elsevier, N.Y., 1981) (both of which are incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. The term "monoclonal anti-

body" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

[0067] Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art. In a non-limiting example, mice can be immunized with an antigen of interest or a cell expressing such an antigen. Once an immune response is detected, e.g., antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells. Hybridomas are selected and cloned by limiting dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding the antigen. Ascites fluid, which generally contains high levels of antibodies, can be generated by inoculating mice intraperitoneally with positive hybridoma clones.

[0068] Antibody fragments which recognize specific epitopes may be generated by known techniques. For example, Fab and F(ab')₂ fragments may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')₂ fragments). F(ab')₂ fragments contain the complete light chain, and the variable region, the CH1 region and the hinge region of the heavy chain.

[0069] The antibodies of the invention or fragments thereof can be also produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques.

[0070] The nucleotide sequence encoding an antibody may be obtained from any information available to those skilled in the art (i.e., from Genbank, the literature, or by routine cloning and sequence analysis). If a clone containing a nucleic acid encoding a particular antibody or an epitope-binding fragment thereof is not available, but the sequence of the antibody molecule or epitope-binding fragment thereof is known, a nucleic acid encoding the immunoglobulin may be chemically synthesized or obtained from a suitable source (e.g., an antibody cDNA library, or a cDNA library generated from, or nucleic acid, preferably poly A+ RNA, isolated from any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, e.g., a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR may then be cloned into replicable cloning vectors using any method well known in the art.

[0071] Once the nucleotide sequence of the antibody is determined, the nucleotide sequence of the antibody may be manipulated using methods well known in the art for the manipulation of nucleotide sequences, e.g., recombinant DNA techniques, site directed mutagenesis, PCR, etc. (see, for example, the techniques described in Sambrook et al., supra; and Ausubel et al., eds., 1998, *Current Protocols in Molecular Biology*, John Wiley & Sons, NY, which are both incorporated by reference herein in their entireties), to generate antibodies having a different amino acid sequence by, for example, introducing amino acid substitutions, deletions, and/or insertions into the epitope-binding domain regions of the antibodies or any portion of antibodies which may enhance or reduce biological activities of the antibodies.

[0072] Recombinant expression of an antibody requires construction of an expression vector containing a nucleotide sequence that encodes the antibody. Once a nucleotide sequence encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof has been obtained, the vector for the production of the antibody molecule may be produced by recombinant DNA technology using techniques well known in the art as discussed in the previous sections. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. The nucleotide sequence encoding the heavy-chain variable region, light-chain variable region, both the heavy-chain and light-chain variable regions, an epitope-binding fragment of the heavy- and/or light-chain variable region, or one or more complementarity determining regions (CDRs) of an antibody may be cloned into such a vector for expression. Thus-prepared expression vector can be then introduced into appropriate host cells for the expression of the antibody. Accordingly, the invention includes host cells containing a polynucleotide encoding an antibody specific for the polypeptides of the invention or fragments thereof.

[0073] The host cell may be co-transfected with two expression vectors of the invention, the first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors may contain identical selectable markers which enable equal expression of heavy and light chain polypeptides or different selectable markers to ensure maintenance of both plasmids. Alternatively, a single vector may be used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to avoid an excess of toxic free heavy chain (Proudfoot, *Nature*, 322:52, 1986; and Kohler, *Proc. Natl. Acad. Sci. USA*, 77:2 197, 1980). The coding sequences for the heavy and light chains may comprise cDNA or genomic DNA.

[0074] In another embodiment, antibodies can also be generated using various phage display methods known in the art. In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In a particular embodiment, such phage can be utilized to display antigen binding domains, such as Fab and Fv or disulfide-bond stabilized Fv, expressed from a repertoire or combinatorial antibody library (e.g., human or murine). Phage expressing an antigen binding domain that binds the antigen of interest can be selected or identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Phage used in these methods are typically filamentous phage, including fd and M13. The antigen binding domains are expressed as a recombinantly fused protein to either the phage gene III or gene VIII protein. Examples of phage display methods that can be used to make the immunoglobulins, or fragments thereof, of the present invention include those disclosed in Brinkman et al., *J. Immunol. Methods*, 182:41-50, 1995; Ames et al., *J. Immunol. Methods*, 184:177-186, 1995; Kettleborough et al., *Eur. J. Immunol.*, 24:952-958, 1994; Persic et al., *Gene*, 187:9-18, 1997; Burton et al., *Advances in Immunology*, 57:191-280, 1994; PCT application No. PCT/GB91/01134; PCT publications WO 90/02809;

WO 91/10737; WO 92/01047; WO 92/18619; WO 93/11236; WO 95/15982; WO 95/20401; and U.S. Pat. Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753; 5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

[0075] As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired fragments, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, e.g., as described in detail below. For example, techniques to recombinantly produce Fab, Fab' and F(ab)₂ fragments can also be employed using methods known in the art such as those disclosed in PCT publication WO 92/22324; Mullinax et al., *BioTechniques*, 12(6):864-869, 1992; and Sawai et al., *AJRI*, 34:26-34, 1995; and Better et al., *Science*, 240:1041-1043, 1988 (each of which is incorporated by reference in its entirety). Examples of techniques which can be used to produce single-chain Fvs and antibodies include those described in U.S. Pat. Nos. 4,946,778 and 5,258,498; Huston et al., *Methods in Enzymology*, 203:46-88, 1991; Shu et al., *PNAS*, 90:7995-7999, 1993; and Skerra et al., *Science*, 240:1038-1040, 1988.

[0076] Once an antibody molecule of the invention has been produced by any methods described above, it may then be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (e.g., ion exchange, affinity, particularly by affinity for the specific antigen after Protein A or Protein G purification, and sizing column chromatography), centrifugation, differential solubility, or by any other standard techniques for the purification of proteins. Further, the antibodies of the present invention or fragments thereof may be fused to heterologous polypeptide sequences described herein or otherwise known in the art to facilitate purification.

[0077] For some uses, including in vivo use of antibodies in humans and in vitro detection assays, it may be preferable to use chimeric, humanized, or human antibodies. A chimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a constant region derived from a human immunoglobulin. Methods for producing chimeric antibodies are known in the art. See e.g., Morrison, *Science*, 229:1202, 1985; Oi et al., *BioTechniques*, 4:214 1986; Gillies et al., *J. Immunol. Methods*, 125:191-202, 1989; U.S. Pat. Nos. 5,807,715; 4,816,567; and 4,816,397, which are incorporated herein by reference in their entireties. Humanized antibodies are antibody molecules from non-human species that bind the desired antigen having one or more complementarity determining regions (CDRs) from the non-human species and framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter, preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, e.g., by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. See, e.g., Queen et al., U.S. Pat. No. 5,585,089; Riechmann et al., *Nature*, 332:323, 1988, which are incorporated herein by reference in their entireties.

Antibodies can be humanized using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; PCT publication WO 91/09967; U.S. Pat. Nos. 5,225,539; 5,530,101 and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, *Molecular Immunology*, 28(4/5):489-498, 1991; Studnicka et al., *Protein Engineering*, 7(6):805-814, 1994; Roguska et al., *Proc Natl. Acad. Sci. USA*, 91:969-973, 1994), and chain shuffling (U.S. Pat. No. 5,565,332), all of which are hereby incorporated by reference in their entireties.

[0078] Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody libraries derived from human immunoglobulin sequences. See U.S. Pat. Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645; WO 98/50433; WO 98/24893; WO 98/16654; WO 96/34096; WO 96/33735; and WO 91/10741, each of which is incorporated herein by reference in its entirety.

[0079] Human antibodies can also be produced using transgenic mice which are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, *Int. Rev. Immunol.*, 13:65-93, 1995. For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; European Patent No. 0 598 877; U.S. Pat. Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825; 5,661,016; 5,545,806; 5,814,318; 5,885,793; 5,916,771; and 5,939,598, which are incorporated by reference herein in their entireties. In addition, companies such as Abgenix, Inc. (Fremont, Calif.), Medarex (NJ) and Genpharm (San Jose, Calif.) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

[0080] Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., *Bio/technology*, 12:899-903, 1988).

[0081] Antibodies fused or conjugated to heterologous polypeptides may be used in in vitro immunoassays and in purification methods (e.g., affinity chromatography) well known in the art. See e.g., PCT publication Number WO 93/21232; EP 439,095; Naramura et al., *Immunol. Lett.*, 39:91-99, 1994; U.S. Pat. No. 5,474,981; Gillies et al., *PNAS*, 89:1428-1432, 1992; and Fell et al., *J. Immunol.*, 146:2446-2452, 1991, which are incorporated herein by reference in their entireties.

[0082] Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the polypeptides of the invention or fragments, derivatives, analogs, or variants thereof, or similar molecules having the similar enzymatic activities as the polypeptide of the invention. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

5.5 Pharmaceutical Compositions and Kits

[0083] The present invention encompasses pharmaceutical compositions comprising anti-viral agents of the present

invention. In a specific embodiment, the anti-viral agent is an antibody which immunospecifically binds CoV-HKU1 or variants thereof, or any proteins derived therefrom. In another specific embodiment, the anti-viral agent is a polypeptide or nucleic acid molecule of the invention. The pharmaceutical compositions have utility as an anti-viral prophylactic agent and may be administered to a subject where the subject has been exposed or is expected to be exposed to a virus.

[0084] Various delivery systems are known and can be used to administer the pharmaceutical composition of the invention, e.g., encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the mutant viruses, receptor mediated endocytosis (see, e.g., Wu and Wu, 1987, *J. Biol. Chem.* 262:4429-4432). Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together with other biologically active agents. Administration can be systemic or local. In a preferred embodiment, it may be desirable to introduce the pharmaceutical compositions of the invention into the lungs by any suitable route. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

[0085] In a specific embodiment, it may be desirable to administer the pharmaceutical compositions of the invention locally to the area in need of treatment; this may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, by means of nasal spray, or by means of an implant, said implant being of a porous, non porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. In one embodiment, administration can be by direct injection at the site (or former site) infected tissues.

[0086] In another embodiment, the pharmaceutical composition can be delivered in a vesicle, in particular a liposome (see Langer, 1990, *Science* 249:1527-1533; Treat et al., in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez Berestein and Fidler (eds.), Liss, New York, pp. 353-365 (1989); Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*).

[0087] In yet another embodiment, the pharmaceutical composition can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, *supra*; Sefton, 1987, *CRC Crit. Rev. Biomed. Eng.* 14:201; Buchwald et al., 1980, *Surgery* 88:507; and Saudek et al., 1989, *N. Engl. J. Med.* 321:574). In another embodiment, polymeric materials can be used (see *Medical Applications of Controlled Release*, Langer and Wise (eds.), CRC Pres., Boca Raton, Fla. (1974); *Controlled Drug Bioavailability, Drug Product Design and Performance*, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, *J. Macromol. Sci. Rev. Macromol. Chem.* 23:61 (1983); see also Levy et al., 1985, *Science* 228:190; During et al., 1989, *Ann. Neurol.* 25:351; Howard et al., 1989, *J. Neurosurg.* 71:105). In yet another embodiment, a controlled release system can be placed in proximity of the composition's target, i.e., the lung, thus requiring only a fraction of the systemic dose (see, e.g.,

Goodson, in *Medical Applications of Controlled Release*, *supra*, vol. 2, pp. 115-138 (1984)).

[0088] Other controlled release systems are discussed in the review by Langer (*Science* 249:1527-1533 (1990)).

[0089] The pharmaceutical compositions of the present invention comprise a therapeutically effective amount of recombinant or chimeric CoV-HKU1, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the pharmaceutical composition is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E. W. Martin. The formulation should suit the mode of administration.

[0090] In a preferred embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

[0091] The pharmaceutical compositions of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with free amino groups such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with free carboxyl groups such as those derived from sodium, potassium,

ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2 ethylamino ethanol, histidine, procaine, etc.

[0092] The amount of the pharmaceutical composition of the invention which will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. However, suitable dosage ranges for intravenous administration are generally about 20-500 micrograms of active compound per kilogram body weight. Suitable dosage ranges for intranasal administration are generally about 0.01 pg/kg body weight to 1 mg/kg body weight. Effective doses may be extrapolated from dose response curves derived from in vitro or animal model test systems.

[0093] Suppositories generally contain active ingredient in the range of 0.5% to 10% by weight; oral formulations preferably contain 10% to 95% active ingredient.

[0094] The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In a preferred embodiment, the kit contains an antiviral agent of the invention, e.g., an antibody specific for the polypeptides encoded by a nucleotide sequence of SEQ ID NO:1 or 3, or any CoV-HKU1 epitope, or a polypeptide or protein of the present invention, including those shown in FIG. 2 (SEQ ID NOS:34-1318), FIG. 8 (SEQ ID NOS:1319-2918), and SEQ ID NO:2, or a nucleic acid molecule of the invention, alone or in combination with adjuvants, antivirals, antibiotics, analgesic, bronchodilators, or other pharmaceutically acceptable excipients.

[0095] The present invention further encompasses kits comprising a container containing a pharmaceutical composition of the present invention and instructions for use.

5.6 Detection Assays

[0096] The present invention provides a method for detecting an antibody, which immunospecifically binds to the CoV-HKU1, in a biological sample, for example blood, serum, plasma, saliva, urine, etc., from a patient suffering from respiratory tract infection. In a specific embodiment, the method comprising contacting the sample with the polypeptides or protein encoded by the nucleotide sequence of SEQ ID NO:1 and/or 3, including the polypeptides having the amino acid sequences of SEQ ID NOS:34-1318 shown in FIG. 2, SEQ ID NOS:1319-2918 shown in FIG. 8, or SEQ ID NO:2, directly immobilized on a substrate and detecting the virus-bound antibody directly or indirectly by a labeled heterologous anti-isotype antibody. In another specific embodiment, the sample is contacted with a host cell comprising a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1 or 3 and expressing the polypeptides encoded thereby, and the bound antibody can be detected by immunofluorescent assay.

[0097] An exemplary method for detecting the presence or absence of a polypeptide or nucleic acid of the invention in a

biological sample involves obtaining a biological sample from various sources and contacting the sample with a compound or an agent capable of detecting an epitope or nucleic acid (e.g., mRNA, genomic RNA) of CoV-HKU1 such that the presence of CoV-HKU1 is detected in the sample. A preferred agent for detecting CoV-HKU1 mRNA or genomic RNA of the invention is a labeled nucleic acid probe capable of hybridizing to mRNA or genomic RNA encoding a polypeptide of the invention. The nucleic acid probe can be, for example, a nucleic acid molecule comprising or consisting of the nucleotide sequence of SEQ ID NO:1 or 3, or a portion thereof, or a complement thereof, such as an oligonucleotide of at least 15, 20, 25, 30, 50, 100, 250, 500, 750, 1,000 or more contiguous nucleotides in length and sufficient to specifically hybridize under stringent conditions to a CoV-HKU1 mRNA or genomic RNA.

[0098] In another preferred specific embodiment, the presence of CoV-HKU1 is detected in the sample by an reverse transcription polymerase chain reaction (RT-PCR) using the primers that are constructed based on a partial nucleotide sequence of the genome of CoV-HKU1 or a genomic nucleic acid sequence of SEQ ID NO:3, or based on a nucleotide sequence of SEQ ID NO: 1. In a non-limiting specific embodiment, preferred primers to be used in a RT-PCR method are: 5'-GGTTGGGACTATCCTAAGTGTGA-3' (SEQ ID NO:4) and 5'-CCATCATCAGATAGAATCATCATA-3' (SEQ ID NO:5), in the presence of 3 mM MgCl₂ and the thermal cycles are, for example, but not limited to, 94° C. for 8 min followed by 40 cycles of 94° C. for 1 min, 50° C. for 1 min, 72° C. for 1 min. In more preferred specific embodiment, the present invention provides a real-time quantitative PCR assay to detect the presence of CoV-HKU1 in a biological sample by subjecting the cDNA obtained by reverse transcription of the extracted total RNA from the sample to PCR reactions using the specific primers, such as those having nucleotide sequences of SEQ ID NOS:4 and 5, and a fluorescence dye, such as SYBR® Green I, which fluoresces when bound non-specifically to double-stranded DNA. The fluorescence signals from these reactions are captured at the end of extension steps as PCR product is generated over a range of the thermal cycles, thereby allowing the quantitative determination of the viral load in the sample based on an amplification plot.

[0099] A preferred agent for detecting CoV-HKU1 is an antibody that specifically binds a polypeptide of the invention or any CoV-HKU1 epitope, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (e.g., Fab or F(ab')₂) can be used.

[0100] The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (i.e., physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin. The detection method of the invention can be used to detect mRNA, protein (or any epitope), or genomic RNA in a sample in vitro as well as in vivo. For example, in vitro techniques for detection of mRNA include northern hybridizations, in situ hybridizations, RT-PCR, and RNase protection. In vitro techniques for detection

of an epitope of CoV-HKU1 include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. In vitro techniques for detection of genomic RNA include northern hybridizations, RT-PCR, and RNase protection. Furthermore, in vivo techniques for detection of CoV-HKU1 include introducing into a subject organism a labeled antibody directed against the polypeptide. For example, the antibody can be labeled with a radioactive marker whose presence and location in the subject organism can be detected by standard imaging techniques, including autoradiography.

[0101] In a specific embodiment, the methods further involve obtaining a control sample from a control subject, contacting the control sample with a compound or agent capable of detecting CoV-HKU1, e.g., a polypeptide of the invention or mRNA or genomic RNA encoding a polypeptide of the invention, such that the presence of CoV-HKU1 or the polypeptide or mRNA or genomic RNA encoding the polypeptide is detected in the sample, and comparing the absence of CoV-HKU1 or the polypeptide or mRNA or genomic RNA encoding the polypeptide in the control sample with the presence of CoV-HKU1, or the polypeptide or mRNA or genomic DNA encoding the polypeptide in the test sample.

[0102] The invention also encompasses kits for detecting the presence of CoV-HKU1 or a polypeptide or nucleic acid of the invention in a test sample. The kit, for example, can comprise a labeled compound or agent capable of detecting CoV-HKU1 or the polypeptide or a nucleic acid molecule encoding the polypeptide in a test sample and, in certain embodiments, a means for determining the amount of the polypeptide or mRNA in the sample (e.g., an antibody which binds the polypeptide or an oligonucleotide probe which binds to DNA or mRNA encoding the polypeptide). Kits can also include instructions for use.

[0103] For antibody-based kits, the kit can comprise, for example: (1) a first antibody (e.g., attached to a solid support) which binds to a polypeptide of the invention or CoV-HKU1 epitope; and, optionally, (2) a second, different antibody which binds to either the polypeptide or the first antibody and is conjugated to a detectable agent.

[0104] For oligonucleotide-based kits, the kit can comprise, for example: (1) an oligonucleotide, e.g., a detectably labeled oligonucleotide, which hybridizes to a nucleic acid sequence encoding a polypeptide of the invention or to a sequence within the CoV-HKU1 genome or (2) a pair of primers useful for amplifying a nucleic acid molecule containing an CoV-HKU1 sequence. The kit can also comprise, e.g., a buffering agent, a preservative, or a protein stabilizing agent. The kit can also comprise components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit can also contain a control sample or a series of control samples which can be assayed and compared to the test sample contained. Each component of the kit is usually enclosed within an individual container and all of the various containers are within a single package along with instructions for use.

6. EXAMPLES

[0105] The following examples illustrate the identification of the novel CoV-HKU1. These examples should not be construed as limiting.

Methods and Results

[0106] As a general reference, Wiedbrauk DL & Johnston SLG. (Manual of Clinical Virology, Raven Press, New York, 1993) was used.

6.1 Clinical Subject

[0107] The patient is an in-patient of the United Christian Hospital in Hong Kong. Nasopharyngeal aspirates were collected from the patient weekly from the first till the fifth week of the illness, stool and urine in the first and second week of the illness, and sera in the first, second, and fourth weeks of the illness.

6.2 Antibody Detection

[0108] To produce a fusion plasmid for protein purification, primers, 5'-TTTTCCTTTT GCGGCCGCTTAAGCAACAGAGTCTTCTA-3' (SEQ ID NO:6) and 5'-CGGAATTC GATGCTTATACTCCCGGT-3'(SEQ ID NO:7) were used to amplify the gene encoding the N protein of the CoV-HKU1 by RT-PCR. The sequence coding for amino acid residues 1 to 441 of the N protein was amplified and cloned into the EcoRI and NotI sites of expression vector pET-28b(+) (Novagen, Madison, Wis., USA) in frame and downstream of the series of six histidine residues. The (His)₆-tagged (SEQ ID NO:27) recombinant N protein was expressed in E. Coli and purified using the Ni²⁺-loaded HiTrap Chelating System (Amersham Pharmacia, USA) according to the manufacturer's instructions.

[0109] Western blot analysis was performed as follows: Two-hundred ng of purified (His)₆-tagged (SEQ ID NO:27) recombinant N protein of CoV-HKU1 were loaded into each well of a sodium dodecyl sulfate (SDS-10% polyacrylamide gel and subsequently electroblotted onto a nitrocellulose membrane (Bio-Rad, Hercules, Calif., USA). The blot was cut into strips and the strips were incubated separately with 1:2000 dilution of serum samples obtained during the first, second, and fourth weeks of the patient's illness. Serum samples of two healthy blood donors were used as controls. Antigen-antibody interaction was detected with an ECL fluorescence system (Amersham Life Science, Buckinghamshire, UK).

[0110] Several prominent immunoreactive bands were visible for serum samples collected during the second and fourth weeks of the patient's illness (FIG. 7, lanes 2 and 3). The sizes of the largest bands were about 53 kDa, consistent with the expected size of 52.8 kDa for the full-length (His)₆-tagged (SEQ ID NO:27) N protein, whereas the other bands were consistent with the degradation products of the (His)₆-tagged (SEQ ID NO:27) N protein. Only very faint bands were observed for serum samples obtained from the patient during the first week of the illness (FIG. 7, lane 1) and two healthy blood donors (FIG. 7, lanes 4 and 5).

[0111] ELISA was performed using the recombinant N protein of CoV-HKU1 prepared as described above. Each well of a Nunc immunoplate (Roskilde, Denmark) was coated with 20 ng of purified (His)₆-tagged (SEQ ID NO:27) recombinant N protein for 12 h and then blocked in phosphate-buffered saline with 2% bovine serum albumin. The serum samples obtained from the patient during the first, second, and fourth weeks of the illness were serially diluted and were added to the wells of the (His)₆-tagged (SEQ ID NO:27) recombinant N protein-coated plates in a total volume of 100 µl per well and incubated at 37° C. for 2 h. After washing with

washing buffer five times, 100 μ l per well of 1:4000 diluted horse radish peroxidase-conjugated goat anti-human IgG antibody (Zymed Laboratories Inc., South San Francisco, Calif., USA) were added to the wells and incubated at 37° C. for 1 h. After washing with washing buffer five times, 100 μ l of diluted 3,3',5,5'-tetramethylbenzidine (Zymed Laboratories Inc.) were added to each well and incubated at room temperature for 15 min. One hundred microliters of 0.3 M H₂SO₄ were added and the absorbance at 450 nm of each well was measured. Each sample was tested in duplicate and the mean absorbance for each serum was calculated.

[0112] Box titration was carried out with different dilutions of (His)₆-tagged (SEQ ID NO:27) recombinant N protein coating antigen and serum obtained from the fourth week of the patient's illness. The results identified 20 ng and 80 ng of purified (His)₆-tagged recombinant N protein per ELISA well as the ideal amount for plate coating and 1:1000 and 1:20 as the most optimal serum dilution for IgG and IgM detection, respectively.

[0113] To establish the baseline for the tests, serum samples (diluted at 1:1000 and 1:20 for IgG and IgM, respectively) from 100 healthy blood donors were tested in the CoV-HKU1 antibody ELISA. For the 100 sera from healthy blood donors, the mean ELISA OD₄₅₀ values for IgG and IgM detection were 0.178 and 0.224, with standard deviations of 0.070 and 0.117. Absorbance values of 0.387 and 0.576 were selected as the cutoff values (that equal the sum of the mean value from the healthy control and three times the standard deviation) for IgG and IgM, respectively. Using these cutoff values, the titers for IgG of the patient's serum samples obtained during the first, second, and fourth weeks of the illness were <1:1000, 1:2000, and 1:8000, respectively (FIG. 6), and those for IgM were 1:20, 1:40, and 1:80, respectively (data not shown).

6.3 RT-PCR and Real Time Quantitative PCR

[0114] RT-PCR Assay

[0115] An RT-PCR was developed to detect the CoV-HKU1 sequence from NPA samples. Total RNA from clinical samples was reverse transcribed using random hexamers and cDNA was amplified using primers 5'-GGTTGGGACTATCCTAAGTGTGA-3'(SEQ ID NO:4) and 5'-CCATCATCAGATAGAATCATCATA-3'(SEQ ID NO:5), which were constructed based on the RNA-dependent RNA polymerase-encoding sequence (SEQ ID NO: 1) of the CoV-HKU1 in the presence of 2.5 mM MgCl₂ (94° C. for 8 min followed by 40 cycles of 94° C. for 1 min, 50° C. for 1 min, 72° C. for 1 min).

[0116] The summary of a typical RT-PCR protocol is as follows:

[0117] 1. RNA Extraction

[0118] RNA from 140 μ l of NPA samples was extracted by QIAquick® viral RNA extraction kit and was eluted in 50 μ l of elution buffer.

[0119] 2. Reverse Transcription

RNA	11.5 μ l
0.1 M DTT	2 μ l
5x buffer	4 μ l
10 mM dNTP	1 μ l
Superscript II, 200 U/ μ l (Invitrogen)	1 μ l
Random hexamers, 0.3 μ g/ μ l	0.5 μ l
Reaction condition	42° C., 50 min 94° C., 3 min 4° C.

[0120] 3. PCR

[0121] cDNA generated by random primers was amplified in a 50 μ l reaction as follows:

cDNA	2 μ l
10 mM dNTP	0.5 μ l
10x buffer	5 μ l
25 mM MgCl ₂	5 μ l
25 μ M Forward primer	0.5 μ l
25 μ M Reverse primer	0.5 μ l
AmpliTaq Gold® polymerase, 5 U/ μ l (Applied Biosystems)	0.25 μ l
Water	36.25 μ l

[0122] Thermal-cycle condition: 95° C., 10 min, followed by 40 cycles of 95° C., 1 min; 50° C. 1 min; 72° C., 1 min.

[0123] 4. Primer Sequences

[0124] Primers were designed based on the RNA-dependent RNA polymerase encoding sequence (SEQ ID NO:1) of the CoV-HKU1.

Forward primer:
(SEQ ID NO: 4)
5'-GGTTGGGACTATCCTAAGTGTGA-3'

Reverse primer:
(SEQ ID NO: 5)
and 5'-CCATCATCAGATAGAATCATCATA-3'
Product size: 440 bps

[0125] Real-Time Quantitative PCR Assay

[0126] Total RNA from 140 μ l of nasopharyngeal aspirate (NPA) was extracted by QIAamp® virus RNA mini kit (Qiagen) as instructed by the manufacturer. Ten μ l of eluted RNA samples were reverse transcribed by 200 U of Superscript® II reverse transcriptase (Invitrogen) in a 20 μ l reaction mixture containing 0.15 μ g of random hexamers, 10 mmol/L DTT, and 0.5 mmol/L dNTP, as instructed. Complementary DNA was then amplified in a SYBR® Green I fluorescence reaction (Roche, Ind.) mixtures. Briefly, 20 μ l reaction mixtures containing 2 μ l of cDNA, 3.5 mmol/L MgCl₂, 0.25 μ mol/L of forward primer [5'-GGTTGGGACTATCCTAAGTGTGA-3' (SEQ ID NO:4)] and 0.25 μ mol/L reverse primer [5'-CCATCATCAGATAGAATCATCATA-3' (SEQ ID NO:5)] were thermal-cycled by a LightCycler® (Roche) with the PCR program, [95° C., 10 min followed by 50 cycles of 95° C., 10 min; 57° C., 5 sec; 72° C. 9 sec]. Plasmids containing the target sequence were used as positive controls. Fluorescence signals from these reactions were captured at the end of extension step in each cycle. To determine the specificity of the assay, PCR products (440 base pairs) were subjected to a melting curve analysis at the end of the assay (65° C. to 95° C., 0.1° C. per second) (data not shown).

[0127] The amount of CoV-HKU1 RNA in the nasopharyngeal aspirates was followed weekly. Quantitative RT-PCR showed that the amounts of CoV-HKU1 RNA were 8.5 \times 10⁵ and 9.6 \times 10⁶ copies per ml in two nasopharyngeal aspirates collected in the first week of the illness, 1.5 \times 10⁵ copies per ml of NPA, respectively, at two time points collected in the second week of the illness, but CoV-HKU1 RNA was undetectable in the NPA collected in the third, fourth and fifth weeks of the illness (FIG. 6). CoV-HKU1 RNA was also

undetectable in the urine and stool of the patient collected in the first and second weeks of the illness.

Discussion

[0128] The genome of CoV-HKU1 is a 29942-nucleotide long, polyadenylated RNA. The G+C content is 32%, which is the lowest among all known coronaviruses with genome sequences available, with a GC skew of 0.19. Table 1 shows the comparison of genomic features of CoV-HKU1 and other corona viruses.

TABLE 1

Coronaviruses	Genome features		
	Size (bases)	G + C content	GC skew
Group 1			
HCoV-229E	27317	0.38	0.13
PEDV	28033	0.42	0.09
HCoV-NL63	27553	0.34	0.16
Group 2			
CoV-HKU1	29942	0.32	0.19
HCoV-OC43	30738	0.37	0.18
BcoV	31028	0.37	0.17
MHV	31357	0.42	0.14
Group 3			
IBV	27608	0.38	0.14
SARS-CoV	29751	0.41	0.02

HCoV-229E = human coronavirus 229E;
 PEDV = porcine epidemic diarrhea virus;
 HCoV-NL63 = human coronavirus NL63;
 HCoV-OC43 = human coronavirus OC43;
 MHV = murine hepatitis virus;
 BCoV = bovine coronavirus;
 IBV = infectious bronchitis virus;
 SARS-CoV = SARS coronavirus;
 GC skew = (G - C)/(G + C)

[0129] The genome organization is the same as other coronaviruses, with the characteristic gene order 5'-replicase, S, E, M, N-3'. Both 5' and 3' ends contain short untranslated regions. The 5' end of the genome consists of a putative 5' leader sequence. A putative transcription regulatory sequences (TRS) motif, 5'-CUAAAC-3', was found at the 3' end of the leader sequence and precedes each translated ORF except ORF4 and ORF6 which encodes the putative E protein. Table 2 shows the putative transcription regulatory sequences in the genome of CoV-HKU1.

TABLE 2

Number of base upstream of AUG	ORF	TRS sequence	SEQ ID NO.
-140	Leader	UUAAAUCUAAACUUUUUAA (127) AUG	8
-7	Hemagglutinin esterase	UUAAAUCUAAACUAUG	9
-6	Spike	UUAAAUCUAAACUAUG	10
-13	ORF 5	UUAAAUCUAAACUUUUUAAUG	11
-9	Membrane	CUAAAUCUAAACAUUAAUG	12

TABLE 2-continued

Number of base upstream of AUG	ORF	TRS sequence	SEQ ID NO.
-13	Nucleocapsid	UUAAAUCUAAACUAUUAGGAUG	13
-35	ORF 9	UUAAAUCUAAACUAUUAGGAUGUCU UAUACUCCCGGUCAUUAAUG	14

[0130] As in SDAV (Sialodacryoadentitis virus) and MHV (mouse hepatitis virus), ORF6 may share the same TRS with ORF 5, suggesting that the translation of the E protein is cap-independent, possibly via an internal ribosomal entry site. The 3' untranslated region contains a predicted pseudoknot structure 59-119 bp downstream of N gene. This pseudoknot structure is highly conserved among coronaviruses and plays a role in coronavirus RNA replication.

[0131] The coding potential of the CoV-HKU1 genome is shown in FIG. 3 and Table 3 and the phylogenetic analyses of the chymotrypsin-like protease (3CL^{pro}), replicase, helicase, haemagglutinin-esterase (HE), S, E, M and N, are shown in FIGS. 4A and 4B.

TABLE 3

ORFs	Start-end (base)	No. of bases	No. of amino acids	Frame	Candidate TRS
ORF 1a	206-13600	13395	4465	+2	—
ORF 1b	13600-21753	8154	2717	+1	—
HE (ORF 2)	21773-22933	1161	386	+2	Strong
S (ORF 3)	22942-27012	4071	1356	+1	Strong
ORF 4	26960-27070	111	36	+2	None
ORF 5	27051-27380	330	109	+3	Strong
E (ORF 6)	27373-27621	249	82	+1	None
M (ORF 7)	27633-28304	672	223	+3	Strong
N (ORF 8)	28320-29645	1326	441	+3	Strong
ORF 9	28342-28959	618	205	+1	Strong

[0132] The replicase 1a ORF (bases 206-13600) and replicase 1b ORF (bases 13600-21753) occupy 21.5 kb of the CoV-HKU1 genome. Similar to other coronaviruses, a frame shift interrupts the protein-coding regions and separates the 1a and 1b ORFs. This ORF encodes a number of putative proteins, including papain-like protease (PLP) with two copies of the PLP domain, PLP1^{pro} and PLP2^{pro}, 3CL^{pro}, replicase, helicase, and other proteins of unknown functions. These proteins are produced by proteolytic cleavages of a large polyprotein (FIG. 3). The sequence of the resulting putative proteins is the same as that in the MHV genome. This polyprotein is synthesized by a -1 ribosomal frameshift at a conserved site (UUUAAAC) upstream of a pseudoknot structure at the junction of ORF 1a and ORF 1b. This ribosomal frameshift would result in a polyprotein of 7182 amino acids, which has 75-77% amino acid identities with the polyprotein in other Group 2 coronaviruses and 43-47% amino acid identities with the polyprotein in other non-Group 2 coronaviruses. The replicase gene of CoV-HKU1, which encodes 928 amino acids, has 87-89% amino acid identities with the replicase of other Group 2 coronaviruses and 54-65% amino acid identities with the replicase of other non-Group 2 coronaviruses (Table 4 and FIG. 4A). Table 4 shows amino acid identities between the predicted chymotrypsin-like protease (3CL^{pro}), replicase (Rep), helicase (Hel), hemagglutinin-es-

terase (HE), spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins of CoV-HKU1 and the corresponding proteins of other coronaviruses.

TABLE 4

Group	Virus	Pairwise amino acid identity (%)							
		3CL ^{pro}	Rep	Hel	HE	S	E	M	N
1	HCoV-229E	45	54	55	—	31	26	35	28
	PEDV	44	56	55	—	30	34	37	37
	PTGV	45	57	57	—	32	34	37	27
	CCoV	—	—	—	—	31	32	36	27
	HCoV-NL63	43	54	54	—	30	28	32	28
2	HCoV-OC43	82	87	88	57	60	54	76	58
	MHV	85	89	87	50	58	55	78	60
	BCoV	84	88	88	56	61	55	76	57
	SDAV	—	—	—	50	61	60	77	62
	ECoV	—	—	—	53	61	56	78	59
	PHEV	—	—	—	54	61	54	77	57
	IBV	41	60	57	—	32	28	38	27
SARS-	SARS-CoV	48	65	63	—	33	27	34	31
CoV									

HCoV-229E = human coronavirus 229E;
 PEDV = porcine epidemic diarrhea virus;
 PTGV = porcine transmissible gastroenteritis virus;
 CCoV = canine enteric coronavirus;
 HCoV-NL63 = human coronavirus NL63;
 HCoV-OC43 = human coronavirus OC43;
 MHV = murine hepatitis virus;
 BCoV = bovine coronavirus;
 SDAV = rat sialodacryoadenitis coronavirus;
 ECov = equine coronavirus NC99;
 PHEV = porcine hemagglutinating encephalomyelitis virus;
 IBV = infectious bronchitis virus;
 SARS-CoV = SARS coronavirus

[0133] The catalytic histidine and cysteine amino acid residues, conserved among the 3CL^{pro} in all coronaviruses, are present in the predicted 3CL^{pro} of CoV-HKU1 (amino acids His³³⁷⁵ and Cys³⁴⁷⁹ of ORF 1a). In the N-terminal of the putative PLP (amino acid residues 945 to 1104 of ORF 1a), there are 14 tandem copies of a 30-base repeat, which encode NNDEEDVVTGD (SEQ ID NO: 15), followed by two 30-base regions that encode NNDEEIVTGD (SEQ ID NO:16) and NDDQIVVTGD (SEQ ID NO:17), located upstream to the first copy of PLP domain, PLP1^{pro}. This repeat is not observed in other coronaviruses.

[0134] ORF 2 (bases 21773-22933) encodes the predicted HE glycoprotein with 386 amino acids. The HE protein of CoV-HKU1 has 50-57% amino acid identities with the HE proteins of other Group 2 coronaviruses (Table 4 and FIG. 4A). PFAM and InterProScan analyses of the ORF show that amino acid residues 1 to 349 of the predicted protein is a member of the haemagglutinin esterase family (PFAM accession no.: PF03996 and INTERPRO accession no. IPR007142). This family contains membrane glycoproteins that are present on viral surface and are involved with the cell infection process. It contains haemagglutinin chain 1 (HE 1) and haemagglutinin chain 2 (HE2), and forms a homotrimer with each monomer being formed by two chains linked by a disulphide bond. Furthermore, PFAM and InterProScan analyses of the ORF show that amino acid residues 122 to 236 of the predicted protein are the haemagglutinin domain of HE-fusion glycoprotein family (PFAM accession no.: PF02710 and INTERPRO accession no. IPR003860). HE is also present in other Group 2 coronaviruses and influenza C virus. SignalP analysis reveals a signal peptide probability of 0.738, with a cleavage site between residues 13 and 14.

Although TMPred and TMHMM analyses of the ORF show four and three transmembrane domains, respectively, PHDhtm analysis of the ORF shows only one transmembrane domain at positions 354 to 376. This concurs with only one transmembrane region reported in the C terminal of the HE of BCoV (bovine coronavirus) and puffinosis virus. PrositeScan analysis of the HE protein of CoV-HKU1 reveals eight potential N-linked glycosylation (six NXS and two NXT) sites. These are located at positions 83 (NYT), 110, (NGS), 145 (NVS), 168 (NYS), 193 (NFS), 286 (NSS), 314 (NVS), and 328 (NFT). The putative active site for neuraminate O-acetyl-esterase activity, FGDS (SEQ ID NO:18), is located at positions 31-34.

[0135] ORF 3 (bases 22942-27012) encodes the predicted S glycoprotein (PFAM accession no. PF01601) with 1356 amino acids. The S protein of CoV-HKU1 has 58-61% amino acid identities with the S proteins of other Group 2 coronaviruses, but has fewer than 35% amino acid identities with the S proteins of Group 1, Group 3, and SARS-CoV (Table 4 and FIG. 4B). InterProScan analysis predicts it as a type I membrane glycoprotein. Important features of the S protein of CoV-HKU1 are depicted in FIG. 5. PrositeScan of the S protein of CoV-HKU1 reveals 28 potential N-linked glycosylation (12 NXS and 16 NXT) sites. SignalP analysis reveals a signal peptide probability of 0.909, with a cleavage site between residues 13 and 14. By multiple alignments with the S proteins of other Group 2 coronaviruses, a potential cleavage site located after RRKRR (SEQ ID NO: 19), between residues 760 and 761, where S will be cleaved into S1 and S2, is identified. Immediately upstream to RRKRR (SEQ ID NO: 19), there is a series of five serine residues that are not present in any other known coronaviruses (FIG. 5). Most of the S protein (residues 15 to 1300) is exposed on the outside of the virus, with a transmembrane domain at the C terminus (TMHMM analysis of the ORF shows one transmembrane domain at positions 1301 to 1356), followed by a cytoplasmic tail rich in cysteine residues. Two heptad repeats (HR), located at residues 982 to 1083 (HR1) and 1250 to 1297 (HR2), identified by multiple alignments with other coronaviruses, are present. In MHV, it has been confirmed that the receptor for its S protein binding is CEACAM1, a member of the carcinoembryonic antigen (CEA) family of glycoproteins in the immunoglobulin superfamily. Furthermore, it has been shown by site-directed mutagenesis, that three conserved regions (sites T, II, and III) and some amino acid residues (Thr⁶², Thr²¹², Tyr²¹⁴, and Tyr²¹⁶ in MHV) in the N-terminal of the S protein are particularly important for its receptor-binding activity. By multiple alignments with the N-terminal 330 amino acids of the S protein of MHV and other group 2 coronaviruses, it is observed that these conserved regions and amino acids are present in CoV-HKU1 (FIG. 5). This infers that the receptor for CoV-HKU1 could be a member of the CEA family on the surface of the cells in the respiratory tract. On the other hand, for HCoV-OC43, it has been shown in vitro that the receptor for the S protein is a sialic acid. However, the amino acid residues on the S protein of HCoV-OC43 that are important for receptor binding are not well defined.

[0136] ORF 4 (bases 26960-27070) encodes a predicted protein with 36 amino acids. This ORF overlaps with the ORF that encodes the S protein. This ORF is not present in other coronaviruses and BlastP analysis of the ORF does not show any hits.

[0137] ORF 5 (bases 27051-27380) encodes a predicted protein with 109 amino acids. This ORF overlaps with the

ORF that encodes the E protein. PFAM analysis of the ORF shows that the predicted protein is a member of the coronavirus non-structural protein NS2 family (PFAM accession no.: PF04753). TMpred and TMHMM analysis do not reveal any transmembrane helix. This predicted protein of CoV-HKU1 has 44-51% amino acid identities with the corresponding proteins of other Group 2 coronaviruses.

[0138] ORF 6 (bases 27373-27621) encodes the predicted E protein with 82 amino acids. The E protein of CoV-HKU1 has 54-60% amino acid identities with the E proteins of other Group 2 coronaviruses, but has fewer than 35% amino acid identities with the E proteins of Group 1, Group 3, and SARS-CoV (Table 4 and FIG. 4B). PFAM and InterProScan analyses of the ORF show that the predicted E protein is a member of the non-structural protein NS3/Small envelope protein E (NS3_envE) family (PFAM accession no.: PF02723). SignalP analysis predicts the presence of a transmembrane anchor (probability 0.995). TMpred analysis of the ORF shows two transmembrane domains at positions 16 to 34 and 39 to 59, and TMHMM analysis of the ORF shows two transmembrane domains at positions 10 to 32 and 39 to 58, consistent with the anticipated association of the E protein with the viral envelope. Both programs predict that both the N and C termini are located on the surface of the virus.

[0139] ORF 7 (bases 27633-28304) encodes the predicted M protein with 223 amino acids. The M protein of CoV-HKU1 has 76-78% amino acid identities with the M proteins of other Group 2 coronavirus, but has fewer than 40% amino acid identities with the M proteins of Group 1, Group 3, and SARS-CoV (Table 4 and FIG. 4B). PFAM analysis of the ORF shows that the predicted M protein is a member of the coronavirus matrix glycoprotein (Corona_M) family (PFAM accession no.: PF01635). SignalP analysis predicts the presence of a transmembrane anchor (probability 0.926). TMpred analysis of the ORF shows three transmembrane domains at positions 21 to 42, 53 to 74, and 77 to 98. TMHMM analysis of the ORF shows three transmembrane domains at positions 20 to 39, 46 to 68, and 78 to 100. The N terminal 19-20 amino acids are located on the outside and the C terminal 123-125-amino acid hydrophilic domain on the inside of the virus.

[0140] ORF 8 (bases 28320-29645) encodes the predicted N protein (PFAM accession no.: PF00937) with 441 amino acids. The N protein of CoV-HKU1 has 57-62% amino acid identities with the N proteins of other Group 2 coronaviruses, but has fewer than 40% amino acid identities with the N proteins of Group 1, Group 3, and SARS-CoV (Table 4 and FIG. 4B).

[0141] ORF 9 (bases 28342-28959) encodes a hypothetical protein (N2) of 205 amino acids within the ORF that encodes the predicted N protein. PFAM analysis of the ORF shows that the predicted protein is a member of the coronavirus nucleocapsid I protein (Corona-1) family (PFAM accession no.: PF03187). This hypothetical N2 protein of CoV-HKU1 has 32-39% amino acid identities with the N2 proteins of other Group 2 coronaviruses.

[0142] We report the characterization and complete genome sequence of a novel coronavirus detected in the nasopharyngeal aspirates of patients with pneumonia. The clinical significance of the virus in the first patient was evident by the high viral loads in the patient's nasopharyngeal aspirates during the first week of his illness, which coincided with the acute symptoms developed in the patient. The viral load decreased during the second week of the illness and was undetectable in the third week of the illness. In addition, the

fall in viral load was accompanied by the recovery from the illness and development of specific antibody response to the recombinant N protein of the virus. Similar to other recently discovered viruses, such as hepatitis C virus, GB virus C, transfusion transmitted virus, and SEN virus, the present virus could not be recovered from cell cultures using the standard cell lines. This could be related to the inherently low recovery rate of coronaviruses. Human coronaviruses are particularly difficult to culture in vitro. Many decades after the recognition of HCoV-229E and HCoV-OC43, there are still only a handful of primary virus isolates available and organ culture is required for primary isolation of HCoV-OC43. In our experience, SARS-CoV can only be recovered from less than 20% of patients with serologically and RT-PCR documented SARS-CoV pneumonia. Therefore, it is not surprising that the new coronavirus CoV-HKU1 has been so far proven difficult to culture in vitro. After the discovery of CoV-HKU1 in the first patient, we conducted a preliminary study on 400 nasopharyngeal aspirates that were collected last year during the SARS epidemic period. Among these 400 nasopharyngeal aspirates, CoV-HKU1 was detected in one specimen, with a viral load comparable to that of the first patient. These results have suggested that CoV-HKU1 is not only incidentally found in one patient, but a previously unrecognized coronavirus associated with pneumomoma.

[0143] Genomic analysis has reveals that CoV-HKU1 is a Group 2 coronavirus. The genome organization of CoV-HKU1 concurs with those of other coronaviruses, with the characteristic gene order, i.e., 5'-replicase, S, E, M, N-3', short untranslated regions in both 5' and 3' ends, 5' conserved coronavirus core leader sequence, putative TRS upstream to multiple ORFs, and conserved pseudoknot in the 3' untranslated region. In contrast to coronaviruses of other groups, CoV-HKU1 contains certain features that are characteristics of Group 2 coronaviruses, including the presence of HE, ORF 5, and N2. Phylogenetic analysis of the 3CL^{pro}, replicase, helicase, S, E, M, and N proteins showed that these genes of CoV-HKU1 were clustered with the corresponding genes in other Group 2 coronaviruses. However, the proteins of CoV-HKU1 formed distinct branches in the phylogenetic trees, indicating that CoV-HKU1 is a distinct member of the group, and is not very closely related to any other known members of Group 2 coronaviruses (FIGS. 4A and 4B).

[0144] In addition to phylogenetic analysis of the putative proteins, CoV-HKU1 exhibits certain features that are distinct from other Group 2 coronaviruses. Compared to other Group 2 coronaviruses, there is a deletion of about 800 bps between the replicase ORF 1b and the HE ORF 2 in CoV-HKU1. In other Group 2 coronaviruses, including MHV, SDAV, HCoV-OC43 and BCoV, an ORF of 798-837 bp (273-278 amino acids) is present between the replicase 1b ORF and the HE ORF 2. This ORF encodes a protein of the coronavirus non-structural protein NS2a family (PFAM accession no.: PF05213). The absence of this ORF in CoV-HKU1 indicates that this is probably a non-essential gene of coronavirus. In addition to the deletion, the N-terminal of the putative PLP in ORF 1a contains 14 tandem copies of a 30-bp repeat that codes for a highly acidic domain. Similar repeats, with different amino acid compositions, have been found in the genomes of human, rat and parasites, but have not been found in other coronaviruses. The function of these repeats is not well understood, although some authors have suggested that the repeats could be important antigens, and their biological role may be related to their special three-dimensional struc-

tures. The vitellaria antigenic protein of *Clonorchis sinensis* contains 23 tandem copies of a 30-bp repeat that codes for DGGAQPPKSG (SEQ ID NO:20). In the case of *Plasmodium falciparum*, it has been shown that the antigenicity of the circumsporozoite protein is due to its repeating epitope structure. It has also been suggested that the tandemly repeated peptide may induce strong humoral immune response in the infected host and thus may also be useful in serological diagnosis. Further experiments should be performed to delineate the antigenic properties, biological role, and possible clinical usefulness of the repeat in the PLP of CoV-HKU1.

[0145] The geographical, political, and economic location of Hong Kong makes it a unique place for the study of emerging infectious disease. Hong Kong, as the gateway of southern China, with thousands of people crossing the border on surface and by air every day, has a high potential of importing and exporting infectious diseases to and from China, countries in Southeast Asia and from the rest of the world. In 1997, the first 18 human cases of avian influenza A H5N1 virus infection were reported in Hong Kong. In early 2003, two cases of human infection caused by avian influenza A (H5N1) that was acquired in Fujian, were diagnosed in Hong Kong, which provided an early warning of the impending disease threat for humans and poultry in Southeast Asia that followed in 2004. For the SARS epidemic, although both epidemiological and genomic evidence revealed that the disease had first occurred in southern China in November 2002, it did not receive as much international attention until the disease was spread to Hong Kong and through Hong Kong to Singapore, Toronto, Vietnam, and the United States of America. As for emerging bacterial infections, 50% of the patients with gas-

troenteritis associated with the recovery of *Laribacter hongkongensis* had recent history of travel to southern China. In this report, one of the patients also had recent history of travel to Shenzhen of China prior to the development of the respiratory illness. We speculate that he might have contacted the virus in Shenzhen. More intensive surveillance of emerging infectious pathogens in this locality is warranted.

7. MARKET POTENTIAL

[0146] The genome of CoV-HKU1 is completely sequenced. This allows the development of various diagnostic tests as described hereinabove. In addition, this virus contains genetic information which is extremely important and valuable for clinical and scientific research applications.

8. EQUIVALENTS

[0147] Those skilled in the art will recognize, or be able to ascertain many equivalents to the specific embodiments of the invention described herein using no more than routine experimentation. Such equivalents are intended to be encompassed by the following claims.

[0148] All publications, patents and patent applications mentioned in this specification are herein incorporated by reference into the specification to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated herein by reference.

[0149] Citation or discussion of a reference herein shall not be construed as an admission that such is prior art to the present invention.

SEQUENCE LISTING

The patent application contains a lengthy "Sequence Listing" section. A copy of the "Sequence Listing" is available in electronic form from the USPTO web site (<http://seqdata.uspto.gov/?pageRequest=docDetail&DocID=US20090305282A1>). An electronic copy of the "Sequence Listing" will also be available from the USPTO upon request and payment of the fee set forth in 37 CFR 1.19(b)(3).

What is claimed:

1. A method for detecting the presence of a first nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1 or a fragment thereof, or a complement thereof in a biological sample, said method comprising:

- (a) contacting the biological sample with a compound that selectively binds to said first nucleic acid molecule; and
- (b) detecting whether the compound binds to said nucleic acid molecule in the sample.

2. The method of claim 1, wherein the compound that binds to said first nucleic acid molecule is a second nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1 or a complement thereof.

3. The method of claim 1, wherein the compound that binds to said first nucleic acid molecule is a second nucleic acid molecule comprising at least 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, or 350 contiguous nucleotides of the nucleotide sequence of SEQ ID NO: 1, or a complement thereof.

4. A method for detecting the presence of a first nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 3 or a fragment thereof or a complement thereof in a biological sample, said method comprising:

- (a) contacting the biological sample with a compound that selectively binds to said first nucleic acid molecule; and
- (b) detecting whether the compound binds to said nucleic acid molecule in the sample.

5. The method of claim 4, wherein the compound that binds to said first nucleic acid molecule is a second nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1 or 3, or a complement thereof.

6. The method of claim 4, wherein the compound that binds to said first nucleic acid molecule is a second nucleic acid molecule comprising at least 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, or 350 contiguous nucleotides of the nucleotide sequence of SEQ ID NO: 1, or a complement thereof.

7. The method of claim 4, wherein the compound that binds to said first nucleic acid molecule is a second nucleic acid

molecule comprising at least 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 2000, 3000, 4000, 5000, 6000, 7000, 8000, 9000, 10000, 11000, 12000, 13000, 14000, 15000, 16000, 17000, 18000, 19000, 20000, 21000, 22000, 23000, 24000, 25000, 26000, 27000, 28000, or 29000 contiguous nucleotides of the nucleotide sequence of SEQ ID NO: 3, or a complement thereof.

8. A method for identifying a subject infected with CoV-HKU1, comprising:

(a) obtaining total RNA from a biological sample obtained from the subject

(b) reverse transcribing the total RNA to obtain cDNA; and
(c) amplifying the cDNA using a set of primers derived from the nucleotide sequence of SEQ ID NO: 1 or 3, or a complement thereof.

9. The method of claim **8**, wherein the set of primers have the nucleotide sequence of SEQ ID NOS: 4 and 5, respectively.

10. The method of claim **8**, wherein the set of primers have the nucleotide sequence of SEQ ID NOS: 6 and 7, respectively.

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